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(54) **CHOLESTEROL OXIDASE MUTANTS,
COMPOSITIONS, DEVICES, KITS AND USES
THEREOF**

(71) Applicants: **Roche Diabetes Care, Inc.,**
Indianapolis, IN (US); **Ultizyme
International, Ltd.,** Tokyo (JP)

(72) Inventors: **Katsuhiko Kojima**, Tokyo (JP);
Kazushige Mori, Tokyo (JP); **Sode Koji**,
Tokyo (JP)

(73) Assignees: **Ultizyme International, Ltd.**, Tokyo
(JP); **Roche Diabetes Care, Inc.**,
Indianapolis, IN (US)

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Primary Examiner — Ganapathirama Raghu

(74) Attorney, Agent, or Firm — Roche Diabetes Care, Inc.

(57) **ABSTRACT**

Compositions, devices, kits and methods are disclosed for assaying cholesterol with a cholesterol oxidase mutant that has been modified at an amino acid residue involved in the active site. The cholesterol oxidase mutant has reduced oxidase activity while substantially maintaining its dehydrogenase activity.

15 Claims, No Drawings

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**CHOLESTEROL OXIDASE MUTANTS,
COMPOSITIONS, DEVICES, KITS AND USES
THEREOF**
**CROSS-REFERENCE TO RELATED
APPLICATIONS**

This patent application is a continuation of Int'l Patent Application No. PCT/EP2012/003574; filed 24 Aug. 2012, which claims the benefit of EP Patent Application No. 11006940.8; filed 25 Aug. 2011. Each patent application is incorporated herein by reference as if set forth in its entirety.

**REFERENCE TO SEQUENCE LISTING
SUBMITTED ELECTRONICALLY**

An official copy of a Sequence Listing is submitted electronically via EFS-Web as an ASCII-formatted Sequence Listing with a file named "27498SequenceListing.txt," created on 14 Jan. 2014, and having a size of 254 KB. The Sequence Listing is filed concurrently with the Specification, is a part thereof and is incorporated herein by reference as if set forth in its entirety.

TECHNICAL FIELD

This disclosure relates generally to chemistry, medicine and molecular biology, and more particularly, it relates to a cholesterol oxidase mutant having a reduced oxidase activity that can be used in a biosensor test strip, enzyme electrode, sensor and/or kit for measuring cholesterol.

BACKGROUND

The concentration of lipoproteins in blood is important in clinical tests. Lipoproteins can be divided into two groups—high density lipoproteins (HDL) and low density lipoproteins (LDL), each of which having different biological functions. As a measure of the lipoprotein content in blood, cholesterol associated with the lipoproteins is measured. In biological samples like blood, cholesterol is present in the lipoproteins in the form of cholesterol esters.

To measure the lipoprotein-associated cholesterol levels, the cholesterol esters are split by enzymes such as cholesterol esterase. Once freed, cholesterol then is determined. The cholesterol concentration in blood may be measured using an enzyme having specificity to cholesterol such as, for example, cholesterol oxidase (ChOx).

ChOx has been isolated from various organisms, and it has been suggested that cholesterol may be analyzed using such enzymes. ChOx is a flavin adenine dinucleotide (FAD)-dependent enzyme that catalyzes a reaction where cholesterol is oxidized to generate cholest-4-en-3-one, thereby generating the reduced form of FAD, FADH₂. FADH₂, in turn, transmits electrons to an electron acceptor and is converted to its oxidized form. In the presence of oxygen, FADH₂ preferentially transmits electrons to oxygen molecules rather than to artificial electron acceptors (also referred to as mediators or electron mediators). Thus, when cholesterol is assayed by ChOx with mediators, the assay results will be greatly affected by the dissolved oxygen level in the reaction system. Such a disadvantage will be particularly noted in clinical tests of blood samples by a point-of-care testing device utilizing an artificial electron acceptor. Therefore, enzymes used for enzyme biosensor test strips employing artificial electron mediators desirably have low activity toward oxygen.

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For the foregoing reason, there is a need for an enzyme, in particular, a ChOx having an activity that is less affected by the dissolved oxygen level.

BRIEF SUMMARY

An inventive concept described herein includes an enzyme, in particular, a ChOx having an activity that is less affected by a dissolved oxygen level. This concept is achieved by reducing the oxidase activity of an enzyme that in its wild-type form predominantly shows an oxidase activity and also by preferably at the same time increasing the enzyme's dehydrogenase activity. As will be described in more detail below, this has been achieved by modifying the wild-type enzyme.

The disclosure describes various ChOx mutants, and it was surprisingly found that a certain type of mutants exhibits reduced oxidase activity while substantially retaining dehydrogenase activity, in particular dye-mediated dehydrogenase activity.

In an aspect, a ChOx mutant is provided. In some instances, the ChOx mutant can be modified at one or more positions such as:

(a) a position corresponding to position 159 of the amino acid sequence set forth in SEQ ID NO: 1 by substituting the amino acid residue Met with an amino acid residue such as Phe, Leu, Val, Cys, Ile, Ala, Gln, Tyr, Lys or Ser or by substituting the amino acid residue Ile with an amino acid residue such as Phe, Leu, Val, Cys, Ala, Gln, Tyr, Lys or Ser;

(b) a position corresponding to position 228 of the amino acid sequence set forth in SEQ ID NO: 1 by substituting the amino acid residue Val, Met or Ile with an amino acid such as Ala, Thr, Lys, Cys, Ser, Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His; and

(c) a position corresponding to position 396 of the amino acid sequence set forth in SEQ ID NO: 1 by substituting the amino acid residue Phe with an amino acid residue such as Trp, Ser, Thr, Lys, Ala, Asn, His or Asp.

Regardless of the substitution, the ChOx mutant has a reduced oxidase activity when compared to a wild-type ChOx. Specifically, the ChOx mutant can have an oxidase activity of about 30% or less than that of the wild-type ChOx and optionally can have an increased dehydrogenase activity when compared to the wild-type ChOx. In some instances, the ChOx mutant has a dehydrogenase activity of about 50% or more when compared to the wild-type ChOx.

In another aspect, an isolated polynucleotide is provided that encodes a ChOx mutant as described herein.

In another aspect, a vector is provided that includes a polynucleotide encoding a ChOx mutant as described herein.

In another aspect, a host cell is provided that is transformed with a vector as described herein.

In another aspect, a device is provided for assaying cholesterol in a sample, where the device includes a modified ChOx as described herein and optionally an electron mediator. In some instances, an enzyme electrode is provided, where the enzyme electrode includes a modified ChOx as described herein that is immobilized on the electrode. In other instances, an enzyme sensor is provided for assaying cholesterol, where the enzyme sensor includes an enzyme electrode as described herein as a working electrode.

In another aspect, a kit is provided for assaying cholesterol in a sample, where the kit includes a modified ChOx as described herein and optionally an electron mediator.

In view of the foregoing, a method is provided for assaying cholesterol, including lipoprotein-associated cholesterol, in a sample. The method can include contacting the sample with a ChOx mutant as described herein and then measuring an

amount of cholesterol oxidized by the modified ChOx. In some instances, the ChOx mutant is incorporated into a device such as a biosensor test strip, enzyme electrode or sensor as described herein.

These and other advantages, effects, features and objects of the inventive concept will become better understood from the description that follows. The description of exemplary embodiments is not intended to limit the inventive concept to the particular forms disclosed, but on the contrary, the intention is to cover all modifications, equivalents and alternatives falling within the spirit and scope of the inventive concept as defined by the embodiments above and the claims below. Reference should therefore be made to the embodiments above and claims below for interpreting the scope of the inventive concept.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The compositions, devices, kits and methods now will be described more fully hereinafter, in which some, but not all embodiments of the inventive concept are shown. Indeed, the compositions, devices, kits and methods may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will satisfy applicable legal requirements.

Likewise, many modifications and other embodiments of the compositions, devices, kits and methods described herein will come to mind to one of skill in the art to which the disclosure pertains having the benefit of the teachings presented in the foregoing description. Therefore, it is to be understood that the compositions, devices, kits and methods are not to be limited to the specific embodiments disclosed and that modifications and other embodiments are intended to be included within the scope of the appended claims. Although specific terms are employed herein, they are used in a generic and descriptive sense only and not for purposes of limitation.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of skill in the art to which the inventive concept pertains. Although any methods and materials similar to or equivalent to those described herein can be used in the practice or testing of the compositions, devices, kits and methods, the preferred methods and materials are described herein.

Moreover, reference to an element by the indefinite article “a” or “an” does not exclude the possibility that more than one element is present, unless the context clearly requires that there be one and only one element. The indefinite article “a” or “an” thus usually means “at least one.”

Overview

Exemplary compositions, devices, kits and methods are provided for measuring cholesterol, including HDL- and LDL-associated cholesterol, and are based upon a ChOx mutant less affected by a dissolved oxygen level. This concept can be achieved at the very least by reducing the oxidase activity of the ChOx mutant when compared to a wild-type ChOx. In addition, the ChOx mutant can be modified to increase its dehydrogenase activity when compared to the wild-type ChOx. This concept is in contrast to current compositions, devices, kits and methods that largely rely on wild-type ChOx.

Such compositions, devices, kits and methods incorporating a ChOx mutant as described herein are useful in a variety of applications. For example, the ChOx mutant may be used for measuring cholesterol or lipoproteins associated with

cholesterol, such as HDL or LDL, which is clinically useful in diagnosing and controlling certain health conditions.

The work described herein is the first to show that the disadvantages noted above can be solved with a ChOx mutant having at least a reduced oxidase activity and optionally an increased dehydrogenase activity. The present inventive concept therefore provides compositions, devices, kits and methods for measuring cholesterol.

Compositions

- 10 Cholesterol Oxidase Mutants: One composition encompassing the inventive concept includes an isolated, ChOx mutant that exhibits decreased oxidase (or Ox) activity when compared to a wild-type ChOx while substantially retaining dehydrogenase (or Dh) activity. In some instances, the ChOx mutant further exhibits an increased Dh activity when compared to the wild-type ChOx.

As used herein, “isolated,” with respect to a polypeptide (and also a polynucleotide), means a molecule (e.g., polypeptide, protein or polynucleotide) isolated from its natural environment or prepared using synthetic methods such as those known to one of skill in the art. Complete purification is not required in either case. The molecules described herein can be isolated and purified from normally associated material in conventional ways, such that in the purified preparation the molecule is the predominant species in the preparation. At the very least, the degree of purification is such that extraneous material in the preparation does not interfere with use of the molecule in the manner disclosed herein. The molecule is at least about 85% pure; alternatively, at least about 90% pure; alternatively, at least about 95% pure; and alternatively, at least about 99% pure.

As used herein, “about” means within a statistically meaningful range of a value or values such as a stated concentration, length, molecular weight, pH, sequence identity, time frame, temperature or volume. Such a value or range can be within an order of magnitude, typically within 20%, more typically within 10%, and even more typically within 5% of a given value or range. The allowable variation encompassed by “about” will depend upon the particular system under study, and can be readily appreciated by one of skill in the art.

As used herein, “mutant,” when used in connection with a polypeptide or protein such as an enzyme, means a variant containing a substitution in one or more of the amino acid residues on the polypeptide or protein at the indicated position(s). Mutant also is used for a polynucleotide encoding such a mutant polypeptide or protein.

As used herein, “a position corresponding to” means the position of an amino acid residue in a query amino acid sequence that is aligned with the amino acid residue in a reference amino acid sequence using software such as AlignX of Vector NTI with default parameters (available from Invitrogen; see, Lu & Moriyama (2004) *Brief Bioinform.* 5:378-88). Thus, “amino acid (AA) residue at a position corresponding to the position Y of the amino acid sequence set forth in SEQ ID NO: X” means the AA residue in a query amino acid sequence that is aligned with AA Y of SEQ ID NO: X when the query amino acid sequence is aligned with SEQ ID NO: X using AlignX of Vector NTI with default parameters. It should be noted that the AA Y of SEQ ID NO: X itself is also encompassed by this term.

As used herein, “oxidase activity” or “Ox activity” means an enzymatic activity of the ChOx mutant to catalyze the oxidation of cholesterol to generate cholest-4-en-3-one by utilizing oxygen as an electron acceptor. The oxidase activity may be assayed by measuring the amount of generated hydrogen peroxide (H_2O_2) by any method known in the art such as, for example, by reagents for H_2O_2 detection such as 4AA/

TODB/POD (4-aminoantipyrine/N,N-bis(4-sulfonylbutyl)-3-methylaniline disodium salt/horseradish peroxidase) or by a platinum (Pt) electrode. In the context of the relative or quantitative activity, the oxidase activity is specifically defined to be the mole amount of the substrate (cholesterol) oxidized per unit time measured by the amount of generated H₂O₂ at about 25° C. in 10 mM PPB, pH 7.0, 1.5 mM TODB, 2 U/ml horseradish peroxidase (POD), and 1.5 mM 4-aminoantipyrine (4AA). The formation of quinoneimine dye may be measured spectrophotometrically at 546 nm.

As used herein, "dehydrogenase activity" or "Dh activity" means an enzymatic activity of the ChOx mutant to catalyze the oxidation of cholesterol to generate cholest-4-en-3-one by utilizing an electron mediator other than oxygen as an electron acceptor. The dehydrogenase activity may be assayed by measuring the amount of electron transferred to the mediator using, for example, mPMS/DCIP (1-methoxy-5-methylphenazinium methylsulfate/2,6-dichloroindophenol), cPES (trifluoro-acetate-1-(3-carboxy-propoxy)-5-ethyl-phenazinium, NA BM31_1144 (N,N-bis-(hydroxyethyl)-3-methoxy-nitrosoaniline hydrochloride, NA BM31_1008 (N,N-bis-hydroxyethyl-4-nitrosoaniline) and N—N-4-dimethyl-nitrosoaniline. In the context of the relative or quantitative activity, the dehydrogenase activity is specifically defined to be the mole amount of the substrate (e.g., cholesterol) oxidized per unit time measured by the amount of electron transferred to the mediator at about 25° C. in 10 mM PPB (pH 7.0), 0.6 mM DCIP, and 6 mM methoxy PMS (mPMS).

The ChOx mutant therefore has a reduced oxidase activity when compared to a wild-type ChOx, while substantially retaining the dehydrogenase activity. The ChOx mutant can have an oxidase activity of about 50% or less when compared to the wild-type ChOx. Alternatively, the ChOx mutant has an oxidase activity of about 40% or less, about 30% or less, about 20% or less, or about 15% or less when compared to the wild-type ChOx.

In addition, the ChOx mutant can have a dehydrogenase activity of about 50% or more when compared to a wild-type ChOx. Alternatively, the ChOx mutant has a dehydrogenase activity of about 60% or more, about 70% or more, about 80% or more, about 90% or more, about 100% or more, or more than 100% or more when compared to the wild-type ChOx.

In the wild-type ChOx, the oxidase activity is about 300 times higher than the dehydrogenase activity. When dissolved oxygen is present in an assay system, electrons generated by oxidizing the substrate can be transferred to oxygen. Thus, the enzyme activity measured in the presence of an electron mediator will be greatly affected by the dissolved oxygen concentration. In contrast, the ChOx mutant as described herein has a ratio of dehydrogenase/oxidase activity of about 2.0 or more, about 4.0 or more, about 6.0 or more, about 8.0 or more, or about 10 or more. Since the dehydrogenase activity exceeds the oxidase activity, the enzyme activity of the ChOx mutant will be less affected by the dissolved oxygen concentration, which is advantageous in utilizing the ChOx mutant in a clinical diagnosis with a blood sample.

It should be understood that the numbering of the amino acid sequence for ChOx herein begins at an initial Met and that the claimed ChOx mutant may or may not have the signal peptide. Examples of amino acid sequences for the ChOx mutant include, but are not limited to, SEQ ID NOS. 1-48 modified at least at one of a position corresponding to position 159, 228 or 396 of SEQ ID NO: 1.

Cholesterol Oxidase Mutant-Encoding Polynucleotides: Another composition encompassing the inventive concept includes an isolated polynucleotide that encodes a ChOx

mutant as described herein. An isolated polynucleotide has a structure that is not identical to that of any naturally occurring nucleic acid molecule or to that of any fragment of a naturally occurring genomic nucleic acid spanning more than one gene.

An isolated polynucleotide also includes, without limitation, (a) a nucleic acid having a sequence of a naturally occurring genomic or extrachromosomal nucleic acid molecule, but which is not flanked by the coding sequences that flank the sequence in its natural position; (b) a nucleic acid incorporated into a vector or into a prokaryote or eukaryote host cell's genome such that the resulting polynucleotide is not identical to any naturally occurring vector or genomic DNA; (c) a separate molecule such as a cDNA, a genomic fragment, a fragment produced by polymerase chain reaction (PCR) or a restriction fragment; and (d) a recombinant nucleotide sequence that is part of a hybrid gene (i.e., a gene encoding a fusion protein). Specifically excluded from this definition are nucleic acids present in mixtures of clones, e.g., as these occur in a DNA library such as a cDNA or genomic DNA library. An isolated polynucleotide can be modified or unmodified DNA or RNA, whether fully or partially single-stranded or double-stranded or even triple-stranded. In addition, an isolated polynucleotide can be chemically or enzymatically modified and can include so-called non-standard bases such as inosine.

The nucleotide sequence of polynucleotides coding for ChOx may be readily obtained from public databases such as, for example, GenBank®, European Nucleotide Archive, DNA Databank of Japan, and Int'l Nucleotide Sequence Database Collaboration.

The polynucleotide encoding the wild-type ChOx may be cloned from the genome of respective organisms using PCR or other known techniques. Then, mutations may be introduced by techniques such as site-directed mutagenesis, PCR mutagenesis or any other known techniques. The amino acid residue to be mutated may be identified using any software for sequence alignment available in the art. Alternatively, polynucleotides coding for the ChOx mutant may be prepared by PCR using a series of chemically synthesized oligonucleotides, or fully synthesized. Examples of nucleotide sequences for the ChOx mutant can include, but are not limited to, those encoding an amino acid sequence as set forth in any one of SEQ ID NOS. 1-48 modified at least at one of a position corresponding to position 159, 228 or 396 of SEQ ID NO: 1.

Vectors and Host Cells: Other compositions encompassing the inventive concept include a vector having the ChOx mutant-encoding polynucleotide or a host cell expressing the vector. The ChOx mutant may be prepared by inserting a mutant polynucleotide into an appropriate expression vector and introducing the vector into an appropriate host cell, such as, for example, *Escherichia coli*. The transformant is cultured and the ChOx mutant expressed in the transformant may be collected from the cells or culture medium by any known technique.

The recombinant ChOx mutant thus obtained may be purified by any of the known purification techniques including, but not limited to, ion exchange column chromatography, affinity chromatography, liquid chromatography, filtration, ultrafiltration, salt precipitation, solvent precipitation, immunoprecipitation, gel electrophoresis, isoelectric electrophoresis and dialysis.

Thus, the inventive concept encompasses isolated or purified polypeptides, proteins and polynucleotides for a ChOx mutant, a vector comprising the polynucleotide encoding the ChOx mutant, a host cell transformed with such a vector, and

a method for preparing the ChOx mutant by culturing the transformant, collecting and purifying the ChOx mutant from the culture.

Devices

In addition to the above compositions, the inventive concept encompasses various devices for assaying cholesterol, including HDL- or LDL-associated cholesterol, in a sample, where the device includes a ChOx mutant as described herein and optionally an electron mediator.

Biosensor Test Strips: One device encompassing the inventive concept includes biosensor test strips having at least the ChOx mutant as described herein as a reagent. The assay device may have a similar structure as any conventional, commercially available electrochemical (e.g., amperometric) biosensor test strip for monitoring the blood cholesterol level. One example of such a device has two electrodes (i.e., a working electrode and a reference or counter electrode) positioned on an insulating substrate, a reagent port and a sample receiver. The reagent port contains the ChOx mutant and the electron mediator.

When a sample, such as a blood sample, is added to the sample receiver, cholesterol contained in the sample will react with the ChOx mutant and the electron mediator to generate a current, which is indicative of the amount of cholesterol in the sample. Examples of electrochemical biosensors for determining enzyme substrate concentration are known in, for example, Int'l Patent Application Publication No. WO 2004/113900 and U.S. Pat. No. 5,997,817.

As an alternative to electrochemical biosensors, optical detection technologies might be used. Typically, such optical devices are based on color changes that occur in a reagent system comprising an enzyme, an electron mediator and an indicator. The color changes can be quantified using fluorescence, absorption or remission measurements. Examples of optical devices for determining enzyme substrate concentration are known in, for example, U.S. Pat. Nos. 7,008,799; 6,036,919 and 5,334,508.

Enzyme Electrodes: Another device encompassing the inventive concept includes an enzyme electrode having at least the ChOx mutant immobilized on the electrode.

Enzyme Sensors: Another device encompassing the inventive concept includes an enzyme sensor for assaying cholesterol having an enzyme electrode as described herein as a working electrode. The concentration of cholesterol in a sample may be determined by measuring the amount of electrons generated by the enzyme reaction. Various sensor systems are known in the art and include, but are not limited to, carbon (C) electrode, metal electrode and Pt electrode.

Here, the ChOx mutant can be immobilized on electrodes. Examples of means for immobilizing molecules such as the ChOx mutant include, but are not limited to, cross-linking, encapsulating into a macromolecular matrix, coating with a dialysis membrane, optical cross-linking polymer, electro-conductive polymer, oxidation-reduction polymer, and any combination thereof.

When the measurement is conducted in an amperometric system using a C electrode, gold (Au) electrode or Pt electrode provided with an immobilized enzyme is used as a working electrode, together with a counter electrode (such as a Pt electrode) and a reference electrode (such as a Ag/AgCl electrode). The electrodes can be inserted into a buffer containing a mediator and kept at predetermined temperature.

A predetermined voltage can be applied to the working electrode, and then a sample is added and an increased value in electric current is measured. Examples of the mediators for use in the assay include, but are not limited to, potassium ferricyanide, ferrocene, osmium derivative, ruthenium

derivative, phenazine methosulfate, etc. It is generally also possible to use so-called two-electrode systems with one working electrode and one counter or pseudo-reference electrode.

Further, cholesterol may be assayed using an immobilized electron mediator in an amperometric system using a C electrode, Au electrode or Pt electrode. The enzyme, such as a ChOx mutant, can be immobilized on the electrode together with an electron mediator such as potassium ferricyanide, ferrocene, osmium derivative, or phenazine methosulfate in a macromolecular matrix by means of adsorption or covalent bond to prepare a working electrode.

The working electrode can be inserted into buffer together with a counter electrode (such as a Pt electrode) and a reference electrode (such as a Ag/AgCl electrode), and kept at a predetermined temperature. As indicated above, a predetermined voltage can be applied to the working electrode, and then the sample is added and increased value in electric current is measured.

It is to be understood that whenever this disclosure refers to cholesterol as an analyte other analytes that can be converted to cholesterol such as, for example, HDL-associated cholesterol or LDL-associated cholesterol, also shall be encompassed. One of skill in the art knows that a cholesterol esterase enzyme may be required to set free cholesterol from cholesterol esters that naturally occur in sample materials like blood or blood fractions.

Thus, the inventive concept encompasses biosensor test strips, electrodes and sensors including at least the ChOx mutant as described herein.

Kits

In addition to the above compositions and devices, the inventive concept encompasses kits for assaying cholesterol, as well as HDL- or LDL-associated cholesterol, in a sample, where the kits include at least a ChOx mutant as described herein and optionally an electron mediator.

Additionally, the kits can include a buffer necessary for the measurement, an appropriate electron mediator and, if necessary, further enzymes such as cholesterol esterase, a standard solution of cholesterol for preparing a calibration curve and an instruction for use. The ChOx mutant may be provided in various forms such as, for example, a freeze-dried reagent or a solution in an appropriate storage solution.

Any or all of the kit reagents can be provided within containers that protect them from the external environment, such as in sealed containers. Positive and/or negative controls can be included in the kits to validate the activity and correct usage of reagents employed in accordance with the inventive concept. Controls can include samples known to be either positive or negative for the presence of a predetermined concentration of cholesterol, HDL-associated cholesterol and/or LDL-associated cholesterol. The design and use of controls is standard and well within the routine capabilities of one of skill in the art.

Methods

In addition to the compositions, devices and kits, the inventive concept encompasses methods of assaying cholesterol, HDL-associated cholesterol and/or LDL-associated cholesterol in a sample.

The method can include at least a step of contacting the sample with the ChOx mutant and a step of measuring the

amount of the cholesterol oxidized by the ChOx mutant as described above and further below.

EXAMPLES

The inventive concept will be more fully understood upon considering the following non-limiting examples, which are offered for purposes of illustration, not limitation.

Example 1

Plasmids Expressing ChOx of *Streptomyces* sp. Strain SA-COO

pET28 ChOx_Nhis was used as a plasmid expressing ChOx of *Streptomyces* sp. strain SA-COO. This plasmid has a DNA fragment of the ChOx structural gene derived from *Streptomyces* sp. strain SA-COO, which is inserted in the NheI/HindIII cloning site of a vector pET28a. The ChOx gene in this plasmid is controlled by a T7 promoter. The pET28 ChOx_Nhis contains a kanamycin resistance gene.

Example 2

Mutagenesis of the ChOx Structural Gene Derived from *Streptomyces* sp. Strain SA-COO

(1). Mutagenesis of Residues 159, 228 and 396.

The *Streptomyces* sp. strain SA-COO-derived ChOx structural gene contained in the pET28 ChOx_Nhis obtained in Example 1 was mutagenized so that Met at residue 159, Val at residue 228, and Phe at residue 396 in ChOx encoded by this gene were substituted by other amino acid residues.

Specifically, the codon (ATG) for Met at residue 159, the codon (GTT) for Val at residue 228, and the codon (TTT) for Phe at residue 396 in the ChOx structural gene contained in the plasmid pET28 ChOx_Nhis described in Example 1 were substituted by other amino acid codons using a commercially available site-directed mutagenesis kit (Stratagene Corp., QuikChange II Site-Directed Mutagenesis Kit).

The sequences of the forward and reverse primers used in the amino acid residue substitution are shown in the tables

below. The number represents a position in the amino acid sequence containing the signal sequence of ChOx; the alphabet described before the number represents an amino acid residue before amino acid substitution; and the alphabet described after the number represents an amino acid residue after amino acid substitution. For example, M159A represents the substitution of Met at residue 159 to Ala.

In a PCR reaction, a reaction solution of the composition shown below was subjected to reaction at 95° C. for 30 seconds and then 15 repetitive cycles each involving 95° C. for 30 seconds, 55° C. for 1 minute and 68° C. for 8 minutes, followed by 68° C. for 30 minutes and then kept at 4° C.

Composition of Reaction Solution:

Template DNA (5 ng/μL)	2 μL
10x reaction buffer	5 μL
Forward primer (100 ng/μL)	1.25 μL
Reverse primer (100 ng/μL)	1.25 μL
dNTP	1 μL
Distilled water	38.5 μL
DNA polymerase	1 μL
Total	50 μL

After the PCR reaction, 0.5 μL of DpnI was added to the reaction solution and incubated at 37° C. for 1 hour to degrade the template plasmid.

E. coli DH5α (supE44, ΔlacU169 (φ80lacZΔM15), hsdR17, recA1, endA1, gyrA96, thi-1, relA1) competent cells were transformed with the obtained reaction solution. From colonies grown on an LB agar medium (1% Bacto tryptone, 0.5% yeast extracts, 1% sodium chloride, 1.5% agar) containing kanamycin (50 μg/mL), plasmid DNA was prepared and sequenced to confirm that the mutation of interest was introduced in the ChOx structural gene.

The plasmid confirmed to have the introduced mutation was digested with restriction enzymes NheI and HindIII to excise the mutagenized ChOx structural gene, which was in turn inserted to a pET28a vector. DH5α was transformed with this plasmid, and a plasmid was extracted from the obtained colonies to obtain a ChOx mutant expression plasmid.

TABLE 1

Forward primer for M159.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
M159A	M159AFw	5' GGTAAACGGTGGCG <u>CGCGCGGTGGAAACCG</u> 3'	49
M159C	M159CFw	5' GGTAAACGGTGG <u>C</u> TGC <u>CGCGGTGGAAACCG</u> 3'	50
M159D	M159DFw	5' GGTAAACGGTGG <u>CGAC</u> CGCGGTGGAAACCG 3'	51
M159E	M159EFw	5' GGTAAACGGTGG <u>CGAAG</u> CGCGGTGGAAACCG 3'	52
M159F	M159FFw	5' GGTAAACGGTGG <u>CTTC</u> CGCGGTGGAAACCG 3'	53
M159G	M159GFw	5' GGTAAACGGTGG <u>CGGT</u> CGCGGTGGAAACCG 3'	54
M159H	M159HFw	5' GGTAAACGGTGG <u>CCAC</u> CGCGGTGGAAACCG 3'	55
M159I	M159IFw	5' GGTAAACGGTGG <u>CATC</u> CGCGGTGGAAACCG 3'	56
M159K	M159KFw	5' GGTAAACGGTGG <u>CAAAG</u> CGCGGTGGAAACCG 3'	57
M159L	M159LFw	5' GGTAAACGGTGG <u>CTTG</u> CGCGGTGGAAACCG 3'	58
M159N	M159NFw	5' GGTAAACGGTGG <u>CAACG</u> CGCGGTGGAAACCG 3'	59

TABLE 1-continued

Forward primer for M159.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
M159P	M159PPw	5' GGTTAACGGTGG <u>CCCGCGGTGGAACCG</u> 3'	60
M159Q	M159QFw	5' GGTTAACGGTGG <u>CCAGGC</u> GGTGGAAACCG 3'	61
M159R	M159RFw	5' GGTTAACGGTGG <u>CTTC</u> CGGGTGGAAACCG 3'	62
M159S	M159SFw	5' GGTTAACGGTGG <u>CT</u> CGGGTGGAAACCG 3'	63
M159T	M159TFw	5' GGTTAACGGTGG <u>CA</u> CCGGGTGGAAACCG 3'	64
M159V	M159VPw	5' GGTTAACGGTGG <u>C</u> GGCGGTGGAAACCG 3'	65
M159W	M159WFw	5' GGTTAACGGTGG <u>CG</u> CGGGTGGAAACCG 3'	66
M159Y	M159YFw	5' GGTTAACGGTGG <u>CTA</u> CGGGTGGAAACCG 3'	67

TABLE 2

Reverse primer for M159.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
M159A	M159ARv	5' CGGTTCCACCG <u>CGCGGCCACC</u> GTTAAC 3'	68
M159C	M159CRv	5' CGGTTCCACCG <u>CGCAGGCCACC</u> GTTAAC 3'	69
M159D	M159DRv	5' CGGTTCCACCG <u>CGTCGCCACC</u> GTTAAC 3'	70
M159E	M159ERv	5' CGGTTCCACCG <u>GTCGCCACC</u> GTTAAC 3'	71
M159F	M159FRv	5' CGGTTCCACCG <u>CGAAGGCCACC</u> GTTAAC 3'	72
M159G	M159GRv	5' CGGTTCCACCG <u>CGACGCCACC</u> GTTAAC 3'	73
M159H	M159HRv	5' CGGTTCCACCG <u>CGTGGCCACC</u> GTTAAC 3'	74
M159I	M159IRv	5' CGGTTCCACCG <u>CGATGCCACC</u> GTTAAC 3'	75
M159K	M159KRv	5' CGGTTCCACCG <u>GTTGCCACC</u> GTTAAC 3'	76
M159L	M159LRv	5' CGGTTCCACCG <u>CGCAGGCCACC</u> GTTAAC 3'	77
M159N	M159NRv	5' CGGTTCCACCG <u>CGTGCACC</u> GTTAAC 3'	78
M159P	M159PRv	5' CGGTTCCACCG <u>CGGGCCACC</u> GTTAAC 3'	79
M159Q	M159QRv	5' CGGTTCCACCG <u>CCTGCCACC</u> GTTAAC 3'	80
M159R	M159RRv	5' CGGTTCCACCG <u>CGAAGGCCACC</u> GTTAAC 3'	81
M159S	M159SRv	5' CGGTTCCACCG <u>CGAGGCCACC</u> GTTAAC 3'	82
M159T	M159TRv	5' CGGTTCCACCG <u>CGGGTGCCACC</u> GTTAAC 3'	83
M159V	M159VRv	5' CGGTTCCACCG <u>CAACGCCACC</u> GTTAAC 3'	84
M159W	M159WRv	5' CGGTTCCACCG <u>CGCCGCCACC</u> GTTAAC 3'	85
M159Y	M159YRv	5' GGTTCCACCG <u>CGTAGGCCACC</u> GTTAAC 3'	86

TABLE 3

Forward primer for V228.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
V228A	V228AFw	5' GGGTACCGTGTT <u>GCCCGAACGTGTATG</u> 3'	87
V228C	V228CFw	5' GGGTACCGTGTT <u>TGCCGAACGTGTATG</u> 3'	88
V228D	V228DFw	5' GGGTACCGTGTT <u>GACCGAACGTGTATG</u> 3'	89
V228E	V228EFw	5' GGGTACCGTGTT <u>GAACCGAACGTGTATG</u> 3'	90
V228F	V228FFw	5' GGGTACCGTGTT <u>TTCCGAACGTGTATG</u> 3'	91
V228G	V228GFw	5' GGGTACCGTGTT <u>GGTCCGAACGTGTATG</u> 3'	92
V228H	V228HFw	5' GGGTACCGTGTT <u>CACCCGAACGTGTATG</u> 3'	93
V228I	V228IFw	5' GGGTACCGTGTT <u>ATCCGAACGTGTATG</u> 3'	94
V228K	V228KFw	5' GGGTACCGTGTT <u>AAACCGAACGTGTATG</u> 3'	95
V228L	V228LFw	5' GGGTACCGTGTT <u>CTCCGAACGTGTATG</u> 3'	96
V228M	V228MFw	5' GGGTACCGTGTT <u>ATGCCGAACGTGTATG</u> 3'	97
V228N	V228NFw	5' GGGTACCGTGTT <u>AAACCGAACGTGTATG</u> 3'	98
V228P	V228PFw	5' GGGTACCGTGTT <u>CCCCGAACGTGTATG</u> 3'	99
V228Q	V228QFw	5' GGGTACCGTGTT <u>CAGCCGAACGTGTATG</u> 3'	100
V228R	V228RFw	5' GGGTACCGTGTT <u>TTCCGAACGTGTATG</u> 3'	101
V228S	V228SFw	5' GGGTACCGTGTT <u>TCTCCGAACGTGTATG</u> 3'	102
V228T	V228TFw	5' GGGTACCGTGTT <u>ACCCGAACGTGTATG</u> 3'	103
V228W	V228WFw	5' GGGTACCGTGTT <u>GGCCGAACGTGTATG</u> 3'	104
V228Y	V228YFw	5' GGGTACCGTGTT <u>TACCCGAACGTGTATG</u> 3'	105

TABLE 4

Reverse primer for V228.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
V228A	V228ARv	5' CATAACGTT <u>CGCGAACACGGTACCC</u> 3'	106
V228C	V228CRv	5' CATAACGTT <u>CGGGCAAAACACGGTACCC</u> 3'	107
V228D	V228DRv	5' CATAACGTT <u>CGGGTCAAACACGGTACCC</u> 3'	108
V228E	V228ERv	5' CATAACGTT <u>CGGTTCAAACACGGTACCC</u> 3'	109
V228F	V228FRv	5' CATAACGTT <u>CGGACCAAACACGGTACCC</u> 3'	110
V228G	V228GRv	5' CATAACGTT <u>CGGACCAAACACGGTACCC</u> 3'	111
V228H	V228HRv	5' CATAACGTT <u>CGGGTCAAACACGGTACCC</u> 3'	112
V228I	V228IRv	5' CATAACGTT <u>CGGGATAAAACACGGTACCC</u> 3'	113
V228K	V228KRv	5' CATAACGTT <u>CGGTTAAACACGGTACCC</u> 3'	114
V228L	V228LRv	5' CATAACGTT <u>CGGCAGAAACACGGTACCC</u> 3'	115
V228M	V228MRv	5' CATAACGTT <u>CGGCATAAAACACGGTACCC</u> 3'	116
V228N	V228NRv	5' CATAACGTT <u>CGGGTAAACACGGTACCC</u> 3'	117
V228P	V228PRv	5' CATAACGTT <u>CGGCAAACACGGTACCC</u> 3'	118
V228Q	V228QRv	5' CATAACGTT <u>CGGCTGAAACACGGTACCC</u> 3'	119

TABLE 4-continued

Reverse primer for V228.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
V228R	V228RRv	5' CATACACGTT <u>CGGGAAA</u> ACACGGTACCC 3'	120
V228S	V228SRv	5' CATACACGTT <u>CGGAGAAA</u> ACACGGTACCC 3'	121
V228T	V228TRv	5' CATACACGTT <u>CGGGTAA</u> ACACGGTACCC 3'	122
V228W	V228WRv	5' CATACACGTT <u>CGGGCAA</u> ACACGGTACCC 3'	123
V228Y	V228YRv	5' CATACACGTT <u>CGGGTAA</u> ACACGGTACCC 3'	124

TABLE 5

Forward primer for F396.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
F396A	F396AFw	5' GATAGCTCTGTT <u>GC</u> GGCCGAAATTGCACC 3'	125
F396C	F396CFw	5' GATAGCTCTGTT <u>GC</u> GCCGAAATTGCACC 3'	126
F396D	F396DFw	5' GATAGCTCTGTT <u>GAC</u> GCCGAAATTGCACC 3'	127
F396E	F396EFw	5' GATAGCTCTGTT <u>GA</u> AGCCGAAATTGCACC 3'	128
F396G	F396GFw	5' GATAGCTCTGTT <u>GG</u> TGCCGAAATTGCACC 3'	129
F396H	F396HFw	5' GATAGCTCTGTT <u>CAC</u> GCCGAAATTGCACC 3'	130
F396I	F396IFw	5' GATAGCTCTGTT <u>ATC</u> GCCGAAATTGCACC 3'	131
F396K	F396KFw	5' GATAGCTCTGTT <u>AA</u> AGCCGAAATTGCACC 3'	132
F396L	F396LFw	5' GATAGCTCTGTT <u>CTG</u> GCCGAAATTGCACC 3'	133
F396M	F396MFw	5' GATAGCTCTGTT <u>ATG</u> GCCGAAATTGCACC 3'	134
F396N	F396NFw	5' GATAGCTCTGTT <u>AAC</u> GCCGAAATTGCACC 3'	135
F396P	F396PFw	5' GATAGCTCTGTT <u>CCG</u> CCGAAATTGCACC 3'	136
F396Q	F396QFw	5' GATAGCTCTGTT <u>CAG</u> CCGAAATTGCACC 3'	137
F396R	F396RFw	5' GATAGCTCTGTT <u>TTG</u> GCCGAAATTGCACC 3'	138
F396S	F396SFw	5' GATAGCTCTGTT <u>CTG</u> GCCGAAATTGCACC 3'	139
F396T	F396TFw	5' GATAGCTCTGTT <u>ACCC</u> CGAAATTGCACC 3'	140
F396V	F396VFw	5' GATAGCTCTGTT <u>GTT</u> GCCGAAATTGCACC 3'	141
F396W	F396WFw	5' GATAGCTCTGTT <u>GGC</u> CCGAAATTGCACC 3'	142
F396Y	F396YFw	5' GATAGCTCTGTT <u>ACCC</u> CGAAATTGCACC 3'	143

TABLE 6

Reverse primer for F396.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
F396A	F396ARv	5' GGTGCAATT <u>TCGGCCG</u> AAACAGAGCTATC 3'	144
F396C	F396CRv	5' GGTGCAATT <u>TCGGCG</u> AAACAGAGCTATC 3'	145
F396D	F396DRV	5' GGTGCAATT <u>TCGGCGT</u> CAACAGAGCTATC 3'	146
F396E	F396ERV	5' GGTGCAATT <u>TCGGCT</u> CAACAGAGCTATC 3'	147

TABLE 6-continued

Reverse primer for F396.			
Amino acid substitution	Primer name	Sequence	SEQ ID NO
F396G	F396GRv	5' GGTGCAATTCGGCACCAACAGAGCTATC 3'	148
F396H	F396HRv	5' GGTGCAATTCGGCGTGAACAGAGCTATC 3'	149
F396I	F396IRv	5' GGTGCAATTCGGCGATAACAGAGCTATC 3'	150
F396K	F396KRv	5' GGTGCAATTCGGCCTTAACAGAGCTATC 3'	151
F396L	F396LRv	5' GGTGCAATTCGGCCAGAACAGAGCTATC 3'	152
F396M	F396MRv	5' GGTGCAATTCGGCCATAACAGAGCTATC 3'	153
F396N	F396NRv	5' GGTGCAATTCGGCGTTAACAGAGCTATC 3'	154
F396P	F396PRv	5' GGTGCAATTCGGCCGGAACAGAGCTATC 3'	155
F396Q	F396QRv	5' GGTGCAATTCGGCCTGAACAGAGCTATC 3'	156
F396R	F396RRv	5' GGTGCAATTCGGCGAAAACAGAGCTATC 3'	157
F396S	F396SRv	5' GGTGCAATTCGGCAGAAAACAGAGCTATC 3'	158
F396T	F396TRv	5' GGTGCAATTCGGCGTAACAGAGCTATC 3'	159
F396V	F396VRv	5' GGTGCAATTCGGCAACAACAGAGCTATC 3'	160
F396W	F396WRv	5' GGTGCAATTCGGCGCAAACAGAGCTATC 3'	161
F396Y	F396YRv	5' GGTGCAATTCGGCGTAAACAGAGCTATC 3'	162

Example 3

Analysis of Enzymatic Activity of ChOx Mutants

Methods:

Mutant ChOx was produced using the mutant ChOx expression plasmid obtained in Example 2, and studied for its enzymatic activity.

(1). Culture.

E. coli strain BL21 (DE3) was transformed with the wild-type ChOx expression plasmid prepared in Example 1 or the mutant ChOx expression plasmid prepared in Example 2. These transformants were separately shake-cultured at 37°C. for 12 hours in 3 mL of an LB medium (containing 50 µg/mL kanamycin) using an L-shaped tube. 1 mL each of these culture solutions was inoculated to a 500-mL Erlenmeyer flask with a baffle containing 100 mL of an LB medium (containing 50 µg/mL kanamycin) and gyratory-cultured at 37°C. At the point in time when OD₆₀₀ reached around 0.6, IPTG (isopropyl-β-D-thiogalactopyranoside) was added thereto at a final concentration of 1 mM, followed by culture at 20°C. for 24 hours.

(2). Preparation of Water-Soluble Fraction.

From the culture solution thus cultured, bacterial cells were collected and washed. Then, the obtained wet bacterial cells were suspended in a 10 mM potassium phosphate buffer (pH 7.0) and sonicated. Then, the homogenate was centrifuged at 17400×g at 4°C. for 20 minutes, and the supernatant was collected. This supernatant was further ultracentrifuged at 100400×g at 4°C. for 60 minutes, and the supernatant was collected. The obtained supernatant was dialyzed against a 10 mM potassium phosphate buffer (pH 7.0), and this was used as a water-soluble fraction. This water-soluble fraction was used as a ChOx sample to determine ChOx and cholesterol dehydrogenase (ChDh) activities for each of wild-type ChOx and mutant ChOx.

(3). Preparation of Substrate Solution.

Cholesterol powder was dissolved at a concentration of 100 mM in Triton X-100 and incubated at 80°C. to completely dissolve cholesterol. The 100 mM cholesterol solution was diluted 10-fold with pure water, cooled in running water, and brought to room temperature. Then, sodium cholate was added thereto at a final concentration of 3 mM to prepare a 10 mM cholesterol solution. For activity determination, the cholesterol solution was appropriately diluted with pure water to prepare various concentrations of substrate solutions.

(4). Determining ChOx Activity.

ChOx activity was determined by quantifying a change in absorbance at 546 nm over time derived from a dye generated using peroxidase, a Trinder reagent (TODB), and 4-aminoantipyrine from H₂O₂ generated through reaction with the substrate. The reaction was performed under conditions shown below.

The reaction was initiated by adding the substrate to a reaction solution (10 mM potassium phosphate buffer pH 7.0+1.5 mM 4-aminoantipyrine+1.5 mM TODB+2 U/ml peroxidase; all the concentrations are final concentrations) containing the enzyme solution, and change in absorbance at 546 nm was determined. Various concentrations of cholesterol were used as the substrate. The amount of an enzyme that forms 1 µmol H₂O₂ for 1 minute is defined as 1 U. 38 mM⁻¹ cm⁻¹ was used as the molar absorption coefficient of TODB at pH 7.0. The formula for calculating an activity value from change in absorbance is shown below.

$$\text{U/ml} = \Delta \text{A} \text{BS}_{546}/\text{min} \times 2/38 \times 10$$

$$\text{U/mg} = \text{U/ml}/\text{protein mg/ml}$$

(5). Determining ChDh Activity.

ChDh activity was determined by quantifying a change in absorbance at 600 nm over time derived from the fading of

DCIP reduced through reaction with the substrate. The reaction was performed under conditions shown below.

The reaction was initiated by adding the substrate to a reaction solution (10 mM potassium phosphate buffer pH 7.0+0.6 mM PMS+0.06 mM DCIP; all the concentrations are final concentrations) containing the enzyme solution, and change in absorbance at 600 nm was determined. Those used in the ChOx activity determination were used as the substrate. The amount of an enzyme that reduces 1 μmol DCIP is defined as 1 U. The activity value was calculated according to the formula shown below. 16.3 mM⁻¹ cm⁻¹ was used as the molar absorption coefficient of DCIP at pH 7.0.

$$\text{U/ml} = \Delta\text{ABS}_{600}/\text{min} \times 1/16.3 \times 5$$

$$\text{U/mg} = \text{U/ml/protein mg/ml}$$

The results of activity determination of the wild-type ChOx and the mutant ChOx are shown in Tables 7-9.

Results:

The oxidase activities of all M159 mutant enzymes were largely reduced. Among them, M159F, M159L and M159V had dehydrogenase activity improved to 1.7 to 2.9 times the wild-type. Particularly, M159F had an oxidase activity value of 2.0×10^{-2} U/mg and a dehydrogenase activity value of 2.2×10^{-2} U/mg, which was 2.9 times the wild-type. The ratio of the dehydrogenase activity to the oxidase activity was 0.28% in the wild-type, whereas this ratio was 110% in M159F, which was improved to approximately 390 times the wild-type.

The oxidase activities of all the V228 mutant enzymes were lower than the wild-type (2.7 U/mg). The mutant that exhibited the lowest activity was V228D (2.0×10^{-4} U/mg). This value was approximately $\frac{1}{1000}$ of the wild-type, showing significantly reduced reactivity to oxygen. In addition to V228D, V228N, V228Q, V228S and V228K exhibited an oxidase activity value as low as 1% or less of the wild-type (V228N: 7.0×10^{-3} U/mg; V228E: 5.0×10^{-3} U/mg; V228S: 9.0×10^{-3} U/mg; and V228K: 8.8×10^{-3} U/mg). On the other hand, the Val228 mutants having substitution to Ile, Leu or Phe, including V228A, had a relatively high oxidase activity value (ratio to wild-type: 10%-) and thus retained reactivity to oxygen (V228I: 2.2 U/mg; V228L: 9.4×10^{-1} U/mg; V228F: 2.2×10^{-1} U/mg).

Eight mutants were obtained that had a dehydrogenase activity improved when compared with the wild-type. Among them, V228T exhibited activity (5.6×10^{-2} U/mg) approximately five times the wild-type. In addition, the mutants having substitution to Lys, Ser or Cys exhibited high dehydrogenase activity (V228K: 3.4×10^{-2} U/mg; V228C, 3.1×10^{-2} U/mg; V228S: 2.0×10^{-2} U/mg). On the other hand, the mutants having substitution to Leu or Ile had activity reduced to $\frac{1}{10}$ of the wild-type (V228L: 1.0×10^{-3} U/mg; V228I: 1.0×10^{-3} U/mg). On the other hand, V228D and V228R had no detectable dehydrogenase activity.

The oxidase activities of the F396 mutant enzymes were reduced. The F396W mutant enzyme had an oxidase activity value of 1.2×10^{-1} U/mg and a dehydrogenase activity value of 2.0×10^{-2} U/mg. The oxidase activity was reduced compared with that of the wild-type ChOx, and the dehydrogenase activity was improved to twice or more the wild-type. The ratio of the dehydrogenase activity to the oxidase activity was 16%, which was 57 times the wild-type (0.28%). F396N and F396D had not only oxidase activity reduced to 1.9% and 0.032%, respectively, of the wild-type, but also dehydrogenase activity reduced to 23% and 14%, respectively, of the wild-type. Each of the mutant enzymes F396M, F396L,

F396V, F396I and F396Y maintained oxidase activity (30% to 80% of the wild-type) when compared with the other mutant enzymes.

TABLE 7

		Ox activity (U/mg)	Dh activity (U/mg)	Dh/Ox (%)
10	WT	2.8 (100%)	7.7×10^{-3} (100%)	0.28
	M159A	3.6×10^{-2} (1.3%)	6.4×10^{-3} (83%)	18
	M159C	2.1×10^{-2} (0.75%)	7.7×10^{-3} (100%)	37
	M159D	7.4×10^{-4} (0.026%)	1.6×10^{-3} (21%)	220
	M159E	4.4×10^{-4} (0.016%)	1.0×10^{-3} (13%)	230
	M159F	2.0×10^{-2} (0.71%)	2.2×10^{-2} (290%)	110
	M159G	1.4×10^{-3} (0.05%)	1.0×10^{-3} (13%)	71
	M159H	6.2×10^{-3} (0.22%)	7.6×10^{-4} (9.9%)	12
	M159I	3.1×10^{-1} (11%)	6.4×10^{-3} (83%)	2.1
	M159K	6.0×10^{-4} (0.021%)	3.0×10^{-3} (39%)	500
	M159L	5.0×10^{-1} (18%)	1.6×10^{-2} (210%)	3.2
	M159N	5.2×10^{-2} (1.9%)	4.2×10^{-4} (5.5%)	0.81
	M159P	1.9×10^{-3} (0.068%)	4.0×10^{-4} (5.2%)	21
	M159Q	3.1×10^{-2} (1.1%)	5.0×10^{-3} (65%)	16
20	M159R	1.5×10^{-4} (0.0054%)	4.8×10^{-4} (6.2%)	320
	M159S	1.8×10^{-1} (6.4%)	2.9×10^{-3} (38%)	1.6
	M159T	2.9×10^{-1} (10%)	2.9×10^{-3} (38%)	1
	M159V	4.7×10^{-2} (1.7%)	1.3×10^{-2} (170%)	28
	M159W	2.3×10^{-2} (0.82%)	3.8×10^{-4} (4.9%)	1.7
	M159Y	7.7×10^{-3} (0.28%)	5.0×10^{-3} (65%)	65

*n.d. = not detected

TABLE 8

		Ox activity (U/mg)	Dh activity (U/mg)	Dh/Ox (%)
30	WT	2.5-2.9	7.0×10^{-3} - 10×10^{-3}	0.25-0.35
	V228A	3.0×10^{-2} - 4.3×10^{-2}	5.7×10^{-2} - 7.4×10^{-2}	150-180
	V228C	7.0×10^{-2}	3.1×10^{-2}	44
	V228D	2.0×10^{-4}	n.d.	—
	V228E	5.0×10^{-3}	1.4×10^{-2}	280
	V228F	2.2×10^{-1}	5.0×10^{-3}	2.3
	V228G	8.0×10^{-3}	1.8×10^{-2}	225
	V228H	1.0×10^{-2}	6.0×10^{-3}	60
	V228I	2.2	1.0×10^{-3}	0.06
	V228K	8.8×10^{-3}	3.4×10^{-2}	374
	V228L	9.4×10^{-1}	1.0×10^{-3}	0.1
	V228M	2.2×10^{-1}	6.0×10^{-4}	0.27
	V228N	7.0×10^{-3}	9.0×10^{-3}	130
	V228P	4.8×10^{-2}	1.2×10^{-2}	25
40	V228Q	2.9×10^{-2}	6.7×10^{-3}	23
	V228R	2.2×10^{-3}	n.d.	—
	V228S	9.0×10^{-3}	2.0×10^{-2}	222
	V228T	1.7×10^{-1}	5.6×10^{-2}	33
	V228W	4.9×10^{-2}	6.2×10^{-3}	13
	V228Y	1.2×10^{-1}	1.3×10^{-2}	110

TABLE 9

		Ox activity (U/mg)	Dh activity (U/mg)	Dh/Ox (%)
55	WT	2.8 (100%)	7.7×10^{-3} (100%)	0.28
	F396A	5.9×10^{-2} (2.1%)	1.8×10^{-3} (23%)	3.1
	F396C	2.2×10^{-1} (7.9%)	2.3×10^{-3} (30%)	1.0
	F396D	8.9×10^{-4} (0.032%)	1.1×10^{-3} (14%)	120
	F396E	2.5×10^{-3} (0.089%)	n.d.	—
	F396G	4.9×10^{-1} (18%)	8.3×10^{-4} (11%)	0.17
	F396H	5.8×10^{-2} (2.1%)	1.5×10^{-3} (19%)	2.6
	F396I	9.7×10^{-1} (35%)	2.3×10^{-3} (30%)	0.24
	F396K	8.9×10^{-2} (3.2%)	3.0×10^{-3} (39%)	3.4
	F396L	1.1 (39%)	2.6×10^{-3} (34%)	0.24
	F396M	8.4×10^{-1} (30%)	5.9×10^{-3} (77%)	0.70
	F396N	5.3×10^{-2} (1.9%)	1.8×10^{-3} (23%)	3.4
	F396P	2.1×10^{-4} (0.0075%)	n.d.	—
60	F396Q	9.6×10^{-4} (0.034%)	n.d.	—
	F396R	3.3×10^{-3} (0.12%)	n.d.	—
	F396S	8.5×10^{-2} (3.0%)	4.1×10^{-3} (53%)	2.7
	F396T	1.9×10^{-1} (6.8%)	3.1×10^{-3} (40%)	1.7

TABLE 9-continued

	Ox activity (U/mg)	Dh activity (U/mg)	Dh/Ox (%)
F396V	7.6×10^{-1} (27%)	2.4×10^{-3} (31%)	0.32
F396W	1.2×10^{-1} (4.3%)	2.0×10^{-2} (260%)	16
F396Y	1.7 (61%)	9.1×10^{-3} (120%)	0.54

Tables 10-12 show alignments of the amino acid sequences that are annotated to be ChOx's. The entire sequences of these ChOx mutants are set forth in SEQ ID NOS: 1-48. Alignment was created using the AlignX application of Vector NTI suite

6.0. One of skill in the art will appreciate that other alignment software programs such as Blast will provide the same or substantially the same alignment.

It is evident from Table 10 that Met159 of SEQ ID NO:1 is conserved among the amino acid sequences listed in Table 10. Accordingly, one of skill in the art can easily identify the Met or Ile residue corresponding to the Met159 of SEQ ID NO:1 within the conserved region using any of commercially available software programs for sequence alignment, and understand that a ChOx mutant is easily prepared by introducing modification on that Met or Ile residue.

TABLE 10

Origin*	Position of mutation		SEQ ID NO**
sp P12676	M159	149 VGGGSLVNGGM A V E PKRSYFE 169	1
gb ABS32193	M155	145 VGGGSLVNGGM A V A PKRSYFE 165	2
ref NP_821583	M160	150 VGGGSLVNGGM A V T P R GYFE 170	3
emb CAC20926	M162	152 VGGGSLVNGGM A V V PKRSYFE 172	4
gb ADX66466	M165	155 VGGGSLVNGGM A V V PKRSYFE 175	5
gb AAR16516	M162	152 VGGGSLVNGGM A V V PKRSYFE 172	6
gb AAZ66744	M165	155 VGGGSLVNGGM A V V P K RAYFE 175	7
gb AAA69655	M160	150 VGGGSLVNGGM A V T P R SYFQ 170	8
ref ZP_07282326	M157	147 VGGGSLVNGAM A V Q PKRSYFE 167	9
ref ZP_07286354	M165	155 VGGGSLVNGGM A P T P R SYFA 175	10
ref ZP_04998002	M166	156 VGGGSLVNGGM S P T P R SYFS 176	11
ref YP_003492288	M154	144 VGGGSLVNGSM A V T P L RSYFA 164	12
gb ADI09201	M158	148 VGGGSLVNGGM A V T P S RAYFQ 168	13
ref ZP_07603147	I164	154 VGGGSLVNGGI A V T PSRSYFQ 174	14
ref YP_003512290	M148	138 VGGGSLVNGGM A V V P R KYFQ 158	15
ref ZP_05008217	M154	144 VGGGSLVNGGM A V T PP P YFS 164	16
ref ZP_06770826	M168	158 VGGGSLVNGGM A V T PP P YFS 178	17
ref ZP_06566730	M151	141 VGGGSLVNGGM A V T P R GYFE 161	18
ref NP_827244	M159	149 VGGGSLVNGGM A V T PLQS Y FA 169	19
ref YP_001108512	M139	129 VGGGSLVNGGM A V T P R GYFE 149	20
ref ZP_07292951	I161	151 VGGGSLVNGGI A V T PPRAYFQ 171	21
ref ZP_07303187	M159	149 VGGGSLVNGGM A V T PLRSYFA 169	22
ref ZP_01689718	M146	136 VGGGSLVNGGM A V T PPMNYFQ 156	23
ref YP_003384280	M157	147 VGGGSLVNGGM A P T P R SYFE 167	24
ref ZP_06916507	M159	149 VGGGSLVNGSM A V T PLQS Y FA 169	25
ref YP_003134867	M150	140 VGGGSLVNGAM A V T PKRATFA 160	26
emb CAC44897	M167	157 VGGGSLVNGGM A V T PKRNYFE 177	27
pdb 1COY_A	M122	112 VGGGSLVNGGM A V T PKRNYFE 132	28
sp P22637	M167	157 VGGGSLVNGGM A V T PKRNYFE 177	29
ref ZP_06830857	M167	157 VGGGSLVNGGM A V T PKRNYFE 177	30
gb ABC75776	M167	157 VGGGSLVNGGM A V T PKRNYFE 177	31

TABLE 10-continued

Origin*	Position of mutation		SEQ ID NO**
gb ABG24169	M167	157 VGGGSLVNG <u>GMAVTPKRN</u> YFE 177	32
emb CAZ68116	M158	148 VGGGSLVNG <u>GMAVTPKRN</u> YFE 168	33
ref YP_002764459	M167	157 VGGGSLVNG <u>GMAVTPKRN</u> YFE 177	34
ref ZP_04388109	M137	127 VGGGSLVNG <u>GMAVTPKRN</u> YFE 147	35
ref YP_003769621	M142	132 VGGGSLVNG <u>GMAVTPKRE</u> NFG 152	36
ref YP_003339891	M166	156 VGGGSLVNG <u>GMAVTPKRE</u> NFG 176	37
ref ZP_07290670	M168	158 VGGGSLVNG <u>GMAVTPKRQ</u> NFA 178	38
ref YP_003116660	M165	155 IGGGSLVNG <u>GMAVTPKQ</u> ENFG 175	39
ref ZP_06588880	M169	159 VGGGSLVNG <u>GMAVTPRRE</u> NFG 179	40
ref ZP_04697978	M121	111 VGGGSLVNG <u>GMAVTPRRE</u> NFG 131	41
ref ZP_06276136	M166	156 VGGGSLVNG <u>GMAVTPRRE</u> NFG 176	42
ref YP_001821989	M166	156 VGGGSLVNG <u>GMAVTPRRE</u> NFG 176	43
ref ZP_05002034	M165	155 VGGGSLVNG <u>GMAVTPKRER</u> FG 175	44
ref ZP_06907496	M166	156 VGGGSLVNG <u>GMAVTPRRE</u> NFG 176	45
ref YP_003100211	M163	153 VGGGSLVNG <u>GMAVTPRRE</u> RFA 173	46
ref ZP_07085639	M142	132 VGGGSLVNG <u>GMAVTPKESY</u> FR 152	47
gb ADX68765	M139	129 VGGGSLVNG <u>GMAVLPKKN</u> YFK 149	48

*Databases: gb: GenBank; sp: Swissprot; ref: RefSeq; emb: EMBL; pdb: Protein Data Bank

**SEQ ID NOS represent the full-length sequence

It is evident from Table 11 that Val228 of SEQ ID NO:1 is conserved among the amino acid sequences listed in Table 11. Accordingly, one of skill in the art can easily identify the Val, Met or Ile residue corresponding to the Val228 of SEQ ID

³⁵ NO:1 within the conserved region using any of commercially available software programs for sequence alignment, and understand that a ChOx mutant is easily prepared by introducing modification on that Val, Met or Ile residue.

TABLE 11

Origin*	Position of mutation		SEQ ID NO**
sp P12676	V228	218 AGKAGLGT <u>VFPNVYDFGYMQ</u> 238	1
gb ABS32193	V224	214 AQKAGLGT <u>VHPNVYDFDHMR</u> 234	2
ref NP_821583	V229	219 ASNAGLST <u>TFVFPNVYDW</u> DYMR 239	3
emb CAC20926	V231	221 AGKAGLTT <u>FVFPNVYDFDY</u> MR 241	4
gb ADX66466	V234	224 AGKAGLST <u>TFVFPNVYDFDY</u> MR 244	5
gb AAR16516	V231	221 AGKAGLST <u>TFVFPNVYDFD</u> HMR 241	6
gb AAZ66744	V234	224 ASKAGLTT <u>TFVFPNVYDFGH</u> MR 244	7
gb AAA69655	V229	219 AENAGLKT <u>TFVFPNVYDW</u> DYMR 239	8
ref ZP_07282326	V226	216 AQKTGLKT <u>TFVFPNVYDFEY</u> YMK 236	9
ref ZP_07286354	V234	224 AQNTGLKT <u>TFVFPNVYDFGY</u> YMK 244	10
ref ZP_04998002	V235	225 AQNTGLKT <u>TFVFPNVYDFEY</u> YMK 245	11
ref YP_003492288	V223	213 AAKAGLRT <u>TFVPSVYDFDH</u> MQ 233	12
gb ADI09201	V227	217 AKTAGLKT <u>TFVFPNVYDFDY</u> MQ 237	13
ref ZP_07603147	M233	223 AARAGLKT <u>TFMPNVYDFDY</u> MR 243	14

TABLE 11-continued

Origin*	Position of mutation		SEQ ID NO**
ref YP_003512290	V217	207 AEETGLATT <u>FV</u> PNVYDFDHMA 227	15
ref ZP_05008217	V223	213 AARAGLGT <u>TVFV</u> PNVYDFDYMR 233	16
ref ZP_06770826	V237	227 AARAGLGT <u>TVFV</u> PNVYDFDYMR 247	17
ref ZP_06566730	V220	210 AQRAGLRTT <u>FV</u> PNVYDFGYMR 230	18
ref NP_827244	V228	218 ATNTGLKTT <u>FV</u> PNVYDFGYMQ 238	19
ref YP_001108512	V208	198 AQRAGLRTT <u>FV</u> PNVYDFGYMR 218	20
ref ZP_07292951	V230	220 ASAAGLKT <u>TVFV</u> PSVYDFDYMR 240	21
ref ZP_07303187	V228	218 ADNAGLKT <u>TFV</u> PNVYDFGHME 238	22
ref ZP_01689718	V215	205 AEKAGFKT <u>TVT</u> VPNIYDYNMQ 225	23
ref YP_003384280	I226	216 AHQAGFR <u>TAVI</u> PNVYDFGYLE 236	24
ref ZP_06916507	V228	218 AQNTGLKTT <u>FV</u> PSVYDFGYMQ 238	25
ref YP_003134867	V219	209 AHNAGLT <u>TTFV</u> PSVYDFARMR 229	26
emb CAC44897	V236	226 AQRSGFTTA <u>FV</u> PNVYDFEYMK 246	27
pdb 1COY_A	V191	181 AQRSGFTTA <u>FV</u> PNVYDFEYMK 201	28
sp P22637	V236	226 AQRSGFTTA <u>FV</u> PNVYDFEYMK 246	29
ref ZP_06830857	V236	226 AQRSGFTTA <u>FV</u> PNVYDFEYMK 246	30
gb ABC75776	V236	226 AQRSGFTTA <u>FV</u> PNVYDFEYMK 246	31
gb ABG24169	V236	226 AQRSGFTTA <u>FV</u> PNVYDFEYMK 246	32
emb CAZ68116	V227	217 AQRSGFTTA <u>FV</u> PNVYDFEYMK 237	33
ref YP_002764459	V236	226 AERSGYTT <u>FV</u> PNVYDFNYMK 246	34
ref ZP_04388109	V206	196 AERSGYTT <u>FV</u> PNVYDFNYMK 216	35
ref YP_003769621	V211	201 AQRSGFP <u>FVFV</u> PDVYDWDMYE 221	36
ref YP_003339891	V235	225 AQRSGFP <u>FVFV</u> PDVYDWDMYE 245	37
ref ZP_07290670	V237	227 AQRSGFP <u>FVFV</u> PDVYDWDMYE 247	38
ref YP_003116660	V234	224 AGRSGFP <u>FQFV</u> PDVYDWNYMQ 244	39
ref ZP_06588880	V238	228 AQRSGFP <u>FLFV</u> PAVYDWDMYE 248	40
ref ZP_04697978	V190	180 AQRSGFP <u>FLFV</u> PAVYDWDMYE 200	41
ref ZP_06276136	V235	225 AQRSGFP <u>FLFV</u> PAVYDWDMYE 245	42
ref YP_001821989	V235	225 AQRSGFP <u>FLFV</u> PAVYDWDMYE 245	43
ref ZP_05002034	V234	224 AQRSGFP <u>FVFV</u> PNVYDWEMYE 244	44
ref ZP_06907496	V235	225 AERSGFP <u>FVFLV</u> PGVYDWDMYE 245	45
ref YP_003100211	V232	222 AQRSGFP <u>FELV</u> PGVYDWAHLE 242	46
ref ZP_07085639	V211	201 AHKAGFKTIR <u>U</u> PNVYDFKYME 221	47
gb ADX68765	V208	198 AQKAGYKTIR <u>U</u> PNVYNFKYME 218	48

*Databases: gb: GenBank; sp: Swissprot; ref: RefSeq; emb: EMBL; pdb: Protein Data Bank

**SEQ ID NOS represent the full-length sequence

It is evident from Table 12 that Phe396 of SEQ ID NO:1 is conserved among the amino acid sequences listed in Table 12. Accordingly, one of skill in the art can easily identify the Phe residue corresponding to the Phe396 of SEQ ID NO:1 within

the conserved region using any of commercially available software programs for sequence alignment, and understand that a ChOx mutant is easily prepared by introducing modification on that Phe residue.

TABLE 12

Origin*	Position of mutation		SEQ ID NO**
sp P12676	F396	386 DAWDN----SDSSV <u>F</u> AEIAPMPAGL 406	1
gb ABS32193	F392	382 DDWDN----PQNPV <u>F</u> AEIAPMPAGL 402	2
ref NP_821583	F397	387 DDWDN----PDTPV <u>F</u> AEIAPLPAGV 407	3
emb CAC20926	F399	389 DDWNN----PTAPV <u>F</u> AEIAPMPAGL 409	4
gb ADX66466	F402	392 DDWDN----PAAPV <u>F</u> AEIAPMPAGL 412	5
gb AAR16516	F399	389 DDWDN----PAAPV <u>F</u> AEIAPMPAGL 409	6
gb AAZ66744	F402	392 DDWNN----AAAPV <u>F</u> AEIAPMPAGA 412	7
gb AAA69655	F397	387 DDWDN----PDNPV <u>F</u> AEIAPMPAGL 407	8
ref ZP_07282326	F394	384 DDWDN----PAHPV <u>F</u> AEIAPVPAGL 404	9
ref ZP_07286354	F402	392 DDWDN----AANPV <u>F</u> AEIAPLPMGI 412	10
ref ZP_04998002	F403	393 DDWDN----AANPV <u>F</u> AEIAPLPMGF 413	11
ref YP_003492288	F391	381 DDWAN----TANPV <u>F</u> AEIAPLPTGL 401	12
gb ADI09201	F395	385 DDWSN----ATNPV <u>F</u> AEIAPLPAGT 405	13
ref ZP_07603147	F401	391 DDWSN----TANPV <u>F</u> AEIAPLPAGL 411	14
ref YP_003512290	F385	375 DDWDN----EAARV <u>F</u> AEIAPVPAGF 395	15
ref ZP_05008217	F397	387 DDWNN----PTHPV <u>F</u> AEIAPLPMGL 407	16
ref ZP_06770826	F411	401 DDWNN----PTHPV <u>F</u> AEIAPLPMGL 421	17
ref ZP_06566730	F388	378 DNWDD----PVHPV <u>F</u> AEIAPLPAGL 398	18
ref NP_827244	F396	386 DDWAN----TSNPV <u>F</u> AEIAPLPMGL 406	19
ref YP_001108512	F376	366 DNWDD----PVHPV <u>F</u> AEIAPLPAGL 386	20
ref ZP_07292951	F398	388 DDWSN----AANPV <u>F</u> AEIAPLPAGT 408	21
ref ZP_07303187	F396	386 DDWAN----TANPV <u>F</u> AEIAPLPAGL 406	22
ref ZP_01689718	F383	373 NDWDN----ASNPV <u>F</u> AEIAPLPTGF 393	23
ref YP_003384280	F393	383 DNWDD----PVHPA <u>F</u> AEIAPLPTGL 403	24
ref ZP_06916507	F396	386 DDWAN----TDNPV <u>F</u> AEIAPLPTGL 406	25
ref YP_003134867	F387	377 DAWD----PRHPV <u>F</u> AEVAPMPAGV 397	26
emb CAC44897	F404	394 DNWAD----PTAPI <u>F</u> AEIAPLPAGL 414	27
pdb 1COY_A	F359	349 DNWAD----PTAPI <u>F</u> AEIAPLPAGL 369	28
sp P22637	F404	394 DNWAD----PTAPI <u>F</u> AEIAPLPAGL 414	29
ref ZP_06830857	F404	394 DNWAD----PTAPI <u>F</u> AEIAPLPAGL 414	30
gb ABC75776	F404	394 DNWAD----PAAP <u>F</u> AEIAPLPAGL 414	31
gb ABG24169	F405	395 DNWAD----PTAPI <u>F</u> AEIAPLPAGL 415	32
emb CAZ68116	F395	385 DNWAD----PTAPI <u>F</u> AEIAPLPAGL 405	33
ref YP_002764459	F405	395 DNWAD----TSAPV <u>F</u> AEIAPFPAGT 415	34
ref ZP_04388109	F375	365 DNWAD----TSAPV <u>F</u> AEIAPFPAGT 385	35
ref YP_003769621	F377	369 DNWAA----GGA-- <u>F</u> AEVAPLPTGI 387	36

TABLE 12-continued

Origin*	Position of mutation		SEQ ID NO**
ref YP_003339891	F401	393 DNWAA---GGA-- <u>FAEVAPLPTGI</u> 411	37
ref ZP_07290670	F403	395 DNWDA---GGA-- <u>FAEVAPLPTGI</u> 413	38
ref YP_003116660	F400	392 DNWTK---GGA-- <u>FAEVAPLPIGI</u> 410	39
ref ZP_06588880	F404	396 DNWDA---GGA-- <u>FAEIAPLPTGI</u> 414	40
ref ZP_04697978	F356	348 DNWDA---GGA-- <u>FAEIAPLPTGI</u> 366	41
ref ZP_06276136	F401	393 DNWDA---GGA-- <u>FAEVAPLPTGI</u> 411	42
ref YP_001821989	F401	393 DNWDA---GGA-- <u>FAEVAPLPTGI</u> 411	43
ref ZP_05002034	F400	392 DNWDA---GGA-- <u>FAEVAPLPTGI</u> 410	44
ref ZP_06907496	F401	393 DNWQA---GGA-- <u>FAEVAPLPTGI</u> 411	45
ref YP_003100211	F397	389 DNWAA---GGA-- <u>FAEVAPLPTGV</u> 407	46
ref ZP_07085639	F380	370 DNWDD---PEHQFFTEIAPLPMGM 390	47
gb ADX68765	F377	367 DNWDD---PKYPFFAEIAPLPMGM 387	48

*Databases: gb: GenBank; sp: Swissprot; ref: RefSeq; emb: EMBL; pdb: Protein Data Bank
 **SEQ ID NOS represent the full-length sequence

All of the patents, patent applications, patent application publications and other publications recited herein are hereby incorporated by reference as if set forth in their entirety.

The present inventive concept has been described in connection with what are presently considered to be the most practical and preferred embodiments. However, the inventive

concept has been presented by way of illustration and is not intended to be limited to the disclosed embodiments. Accordingly, one of skill in the art will realize that the inventive concept is intended to encompass all modifications and alternative arrangements within the spirit and scope of the inventive concept as set forth in the appended claims.

 SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 162

<210> SEQ ID NO 1

<211> LENGTH: 546

<212> TYPE: PRT

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<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (159)..(159)

<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln, Tyr, Lys or Ser

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (228)..(228)

<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser, Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (396)..(396)

<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His or Asp, provided that when Xaa159 is Met, then Xaa396 is not Phe

<400> SEQUENCE: 1

Met Thr Ala Gln Gln His Leu Ser Arg Arg Arg Met Leu Gly Met Ala
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Ala Phe Gly Ala Ala Ala Leu Ala Gly Gly Thr Thr Ile Ala Ala Pro
 20 25 30

Arg Ala Ala Ala Ala Lys Ser Ala Ala Asp Asn Gly Gly Tyr Val
 35 40 45

Pro Ala Val Val Ile Gly Thr Gly Tyr Ala Ala Val Ser Ala Leu
 50 55 60

-continued

Arg Leu Gly Glu Ala Gly Val Gln Thr Leu Met Leu Glu Met Gly Gln
 65 70 75 80

Leu Trp Asn Gln Pro Gly Pro Asp Gly Asn Ile Phe Cys Gly Met Leu
 85 90 95

Asn Pro Asp Lys Arg Ser Ser Trp Phe Lys Asn Arg Thr Glu Ala Pro
 100 105 110

Leu Gly Ser Phe Leu Trp Leu Asp Val Val Asn Arg Asn Ile Asp Pro
 115 120 125

Tyr Ala Gly Val Leu Asp Arg Val Asn Tyr Asp Gln Met Ser Val Tyr
 130 135 140

Val Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala
 145 150 155 160

Val Glu Pro Lys Arg Ser Tyr Phe Glu Glu Ile Leu Pro Arg Val Asp
 165 170 175

Ser Ser Glu Met Tyr Asp Arg Tyr Phe Pro Arg Ala Asn Ser Met Leu
 180 185 190

Arg Val Asn His Ile Asp Thr Lys Trp Phe Glu Asp Thr Glu Trp Tyr
 195 200 205

Lys Phe Ala Arg Val Ser Arg Glu Gln Ala Gly Lys Ala Gly Leu Gly
 210 215 220

Thr Val Phe Xaa Pro Asn Val Tyr Asp Phe Gly Tyr Met Gln Arg Glu
 225 230 235 240

Ala Ala Gly Glu Val Pro Lys Ser Ala Leu Ala Thr Glu Val Ile Tyr
 245 250 255

Gly Asn Asn His Gly Lys Gln Ser Leu Asp Lys Thr Tyr Leu Ala Ala
 260 265 270

Ala Leu Gly Thr Gly Lys Val Thr Ile Gln Thr Leu His Gln Val Lys
 275 280 285

Thr Ile Arg Gln Thr Lys Asp Gly Gly Tyr Ala Leu Thr Val Glu Gln
 290 295 300

Lys Asp Thr Asp Gly Lys Leu Leu Ala Thr Lys Glu Ile Ser Cys Arg
 305 310 315 320

Tyr Leu Phe Leu Gly Ala Gly Ser Leu Gly Ser Thr Glu Leu Leu Val
 325 330 335

Arg Ala Arg Asp Thr Gly Thr Leu Pro Asn Leu Asn Ser Glu Val Gly
 340 345 350

Ala Gly Trp Gly Pro Asn Gly Asn Ile Met Thr Ala Arg Ala Asn His
 355 360 365

Met Trp Asn Pro Thr Gly Ala His Gln Ser Ser Ile Pro Ala Leu Gly
 370 375 380

Ile Asp Ala Trp Asp Asn Ser Asp Ser Ser Val Xaa Ala Glu Ile Ala
 385 390 395 400

Pro Met Pro Ala Gly Leu Glu Thr Trp Val Ser Leu Tyr Leu Ala Ile
 405 410 415

Thr Lys Asn Pro Gln Arg Gly Thr Phe Val Tyr Asp Ala Ala Thr Asp
 420 425 430

Arg Ala Lys Leu Asn Trp Thr Arg Asp Gln Asn Ala Pro Ala Val Asn
 435 440 445

Ala Ala Lys Ala Leu Phe Asp Arg Ile Asn Lys Ala Asn Gly Thr Ile
 450 455 460

Tyr Arg Tyr Asp Leu Phe Gly Thr Gln Leu Lys Ala Phe Ala Asp Asp
 465 470 475 480

Phe Cys Tyr His Pro Leu Gly Gly Cys Val Leu Gly Lys Ala Thr Asp

-continued

485	490	495
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Asp Tyr Gly Arg Val Ala Gly Tyr Lys Asn Leu Tyr Val Thr Asp Gly
500 505 510

Ser Leu Ile Pro Gly Ser Val Gly Val Asn Pro Phe Val Thr Ile Thr
515 520 525

Ala Leu Ala Glu Arg Asn Val Glu Arg Ile Ile Lys Gln Asp Val Thr
530 535 540

Ala Ser
545

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<210> SEQ_ID NO 2
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<212> TYPE: PRT
<213> ORGANISM: Streptomyces virginiae
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<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (155)..(155)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (224)..(224)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (392)..(392)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa155 is Met, then Xaa392 is not Phe
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<400> SEQUENCE: 2

Met Glu Gln His Leu Ser Arg Arg Arg Leu Leu Gly Met Thr Ala Leu
1 5 10 15

Gly Ala Ala Ala Leu Ala Gly Ser Thr Thr Ile Gly Ala Pro Arg Ala
20 25 30

Leu Ala Ala Asp Arg Ala Asp Gly Val Ala Phe Phe Pro Ala Val Val
35 40 45

Ile Gly Thr Gly Tyr Gly Ala Ala Val Ser Ala Leu Arg Leu Gly Glu
50 55 60

Ala Gly Val Arg Thr Val Met Leu Glu Met Gly Gln Leu Trp Asn Gln
65 70 75 80

Pro Gly Pro Asp Gly Asn Val Phe Ala Gly Met Leu Lys Pro Asp Lys
85 90 95

Arg Ser Ser Trp Phe Lys Asn Arg Thr Glu Ala Pro Leu Gly Ser Phe
100 105 110

Leu Trp Leu Asp Leu Ala Asn Arg Asp Ile Asp Pro Tyr Ala Gly Val
115 120 125

Leu Asp Arg Val Asn Phe Asp Gln Met Ser Val Tyr Val Gly Arg Gly
130 135 140

Val Gly Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Ala Pro Lys
145 150 155 160

Arg Ser Tyr Phe Glu Glu Val Leu Pro Arg Val Asp Ser Ala Glu Met
165 170 175

Tyr Ser Arg Tyr Phe Pro Arg Ala Asn Ser Met Leu Arg Val Asn His
180 185 190

Ile Asp Asp Gly Trp Phe Glu Ser Thr Glu Trp Tyr Lys Phe Ala Arg
195 200 205

Val Ser Arg Asp Gln Ala Gln Lys Ala Gly Leu Gly Thr Val His Xaa
210 215 220

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Pro Asn Val Tyr Asp Phe Asp His Met Arg Arg Glu Ala Ala Gly Glu
 225 230 235 240
 Ala Pro Lys Ser Ala Leu Ala Gly Glu Val Ile Tyr Gly Asn Asn His
 245 250 255
 Gly Lys Gln Ser Leu Asp Lys Thr Tyr Leu Ala Ala Ala Leu Gly Thr
 260 265 270
 Gly Lys Val Thr Ile Glu Thr Leu His Gln Ala Arg Thr Ile Arg Gln
 275 280 285
 Gln Lys Asp Gly Thr Tyr Leu Leu Thr Val Glu Gln Arg Asp Ala Asp
 290 295 300
 Gly Arg Leu Leu Ala Thr Lys Glu Ile Ser Cys Arg His Leu Phe Leu
 305 310 315 320
 Gly Ala Gly Ser Leu Gly Ser Thr Glu Leu Leu Leu Arg Ala Arg Glu
 325 330 335
 Thr Gly Thr Leu Pro Asp Leu Ser Ser Glu Ile Gly Ala Gly Trp Gly
 340 345 350
 Pro Asn Gly Asn Ile Met Thr Ala Arg Ala Asn His Val Trp Asn Pro
 355 360 365
 Thr Gly Ala Asn Gln Ser Ser Ile Pro Ala Leu Gly Ile Asp Asp Trp
 370 375 380
 Asp Asn Pro Gln Asn Pro Val Xaa Ala Glu Ile Ala Pro Met Pro Ala
 385 390 395 400
 Gly Leu Glu Thr Trp Val Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro
 405 410 415
 Glu Arg Gly Thr Phe Ala Tyr Asp Ala Ala Thr Asp Arg Ala Ala Leu
 420 425 430
 Arg Trp Thr Arg Asp Gln Asn Thr Pro Ala Val Ser Ala Ala Lys Ser
 435 440 445
 Leu Phe Asp Arg Ile Asn Lys Ala Asn Thr Thr Met Tyr Arg Tyr Asp
 450 455 460
 Leu Phe Gly Lys Gln Leu Lys Ala Phe Ser Asp Asp Phe Thr Tyr His
 465 470 475 480
 Pro Leu Gly Gly Cys Val Leu Gly Arg Ala Thr Asp Asp Tyr Gly Arg
 485 490 495
 Val Lys Gly Tyr Lys Asn Leu Tyr Val Thr Asp Gly Ser Leu Ile Pro
 500 505 510
 Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu
 515 520 525
 Arg Asn Ile Glu Arg Val Ile Arg Gln Asp Val Thr Ala Ala
 530 535 540

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<210> SEQ_ID NO 3
<211> LENGTH: 547
<212> TYPE: PRT
<213> ORGANISM: Streptomyces avermitilis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (160)..(160)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
  Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (229)..(229)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
  Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (397)..(397)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
  
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-continued

or Asp, provided that when Xaa160 is Met, then Xaa397 is not Phe

<400> SEQUENCE: 3

Met Ile Ala His Gln Pro Leu Ser Arg Arg Arg Met Leu Gly Val Ala
1 5 10 15

Ala Leu Gly Ala Ala Ala Leu Ala Gly Gln Thr Thr Ile Thr Ala Ala
20 25 30

Pro Arg Ala Ala Ala Ala Thr Ala Thr Ser Gly Ser Gly Gly Thr Phe
35 40 45

Val Pro Ala Val Val Val Gly Thr Gly Tyr Gly Ala Ala Val Ser Ala
50 55 60

Leu Arg Leu Gly Glu Ala Gly Val Pro Thr Leu Met Leu Glu Met Gly
65 70 75 80

Arg Leu Trp Asn Gln Pro Gly Pro Asp Gly Asn Val Phe Ser Gly Met
85 90 95

Leu Lys Pro Asp Lys Arg Ser Ser Trp Phe Lys Thr Arg Thr Glu Ala
100 105 110

Pro Leu Gly Ser Phe Leu Trp Leu Asp Leu Ala Asn Arg Asp Ile Glu
115 120 125

Pro Tyr Ala Gly Val Leu Asp Arg Val Asn Phe Asp Gln Met Ser Val
130 135 140

Tyr Leu Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly Gly Xaa
145 150 155 160

Ala Val Thr Pro Arg Arg Ser Tyr Phe Glu Glu Val Leu Pro Gln Val
165 170 175

Asp Ala Glu Glu Met Tyr Thr Lys Tyr Phe Pro Arg Ala Asn Ser Thr
180 185 190

Leu Arg Val Asn Asn Ile Asp Lys Ser Trp Phe Glu Gln Thr Asp Trp
195 200 205

Tyr Ser Phe Ala Arg Val Ser Arg Arg Gln Ala Ser Asn Ala Gly Leu
210 215 220

Ser Thr Thr Phe Xaa Pro Asn Val Tyr Asp Trp Asp Tyr Met Arg Arg
225 230 235 240

Glu Ala Asp Gly Ala Val Pro Lys Ser Ala Leu Ala Ala Glu Val Ile
245 250 255

Tyr Gly Asn Asn His Gly Lys Val Ser Leu Asp Lys Ser Tyr Leu Ala
260 265 270

Ala Ala Leu Gly Thr Gly Lys Val Thr Ile Glu Thr Leu His Gln Val
275 280 285

Lys Thr Ile Arg Gln Gln Asn Asp Gly Thr Tyr Leu Leu Thr Val Glu
290 295 300

Gln Arg Asp Thr Gly Gly Lys Leu Leu Gly Thr Lys Glu Val Ser Cys
305 310 315 320

Arg His Leu Phe Leu Gly Ala Gly Ser Leu Gly Ser Thr Glu Leu Leu
325 330 335

Leu Arg Ala Arg Glu Thr Gly Thr Leu Pro Gly Leu Ser Pro Glu Val
340 345 350

Gly Gly Gly Trp Gly Pro Asn Gly Asn Ile Met Thr Ala Arg Ala Asn
355 360 365

His Met Trp Asn Pro Thr Gly Thr Lys Gln Ser Ser Ile Pro Ala Leu
370 375 380

Gly Ile Asp Asp Trp Asp Asn Pro Asp Thr Pro Val Xaa Ala Glu Ile
385 390 395 400

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Ala Pro Leu Pro Ala Gly Val Glu Thr Trp Val Ser Leu Tyr Leu Ala
405 410 415

Ile Thr Lys Asn Pro Glu Arg Gly Thr Phe Val Tyr Asp Ala Ala Lys
420 425 430

Asp Arg Ala Asp Leu Arg Trp Thr Arg Asp Gln Asn Ala Pro Ala Ile
435 440 445

Ala Ala Ala Lys Ser Leu Phe Asp Arg Ile Asn Lys Ala Asn Ala Thr
450 455 460

Ile Tyr Arg Tyr Asp Leu Phe Gly Lys Gln Ile Lys Ala Phe Ala Asp
465 470 475 480

Asp Phe Cys Tyr His Pro Leu Gly Gly Cys Val Leu Gly Lys Ala Thr
485 490 495

Asp Asp Tyr Gly Arg Val Thr Gly Tyr Lys Asn Leu Tyr Val Thr Asp
500 505 510

Gly Ser Leu Ile Pro Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile
515 520 525

Ala Ala Leu Ala Glu Arg Asn Ile Glu Arg Val Ile Lys Gln Asp Ile
530 535 540

Ala Asp Ser
545

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<210> SEQ_ID NO 4
<211> LENGTH: 549
<212> TYPE: PRT
<213> ORGANISM: Streptomyces natalensis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (162)..(162)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (231)..(231)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (399)..(399)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa162 is Met, then Xaa399 is not Phe
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<400> SEQUENCE: 4

Met Phe Glu Asn Gln His Leu Ser Arg Arg Arg Leu Leu Gly Leu Ala
1 5 10 15

Ala Leu Gly Gly Ala Ala Ala Ala Gly Met Thr Thr Ile Thr Ser Ala
20 25 30

Pro His Ala Ala Ala Ala Asp Arg Arg Ser Pro Gln Ala Arg Ser Gly
35 40 45

Ser Phe Val Pro Ala Val Val Ile Gly Thr Gly Tyr Gly Ala Ala Val
50 55 60

Ser Ala Leu Arg Leu Gly Glu Ala Gly Ile Pro Thr Leu Met Leu Glu
65 70 75 80

Met Gly Gln Leu Trp Asn Lys Pro Ala Asp Asp Gly Asn Val Phe Cys
85 90 95

Gly Met Leu Ser Pro Asp Arg Arg Ser Ser Trp Phe Lys Ser Arg Thr
100 105 110

Glu Ala Pro Leu Gly Ser Phe Leu Trp Leu Asp Val Ile Asn Arg Asp
115 120 125

Ile Asp Pro Tyr Ala Gly Val Leu Asp Lys Val His Phe Asp Gln Met
130 135 140

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Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly
 145 150 155 160
 Gly Xaa Ala Val Val Pro Lys Arg Ser Tyr Phe Glu Glu Val Leu Pro
 165 170 175
 Arg Val Asp Ala Ala Glu Met Tyr Asp Arg Tyr Phe Pro Arg Ala Asn
 180 185 190
 Ser Met Leu Lys Val Asn His Ile Asp Lys Gly Trp Phe Glu Glu Thr
 195 200 205
 Glu Trp Tyr Lys Phe Ala Arg Val Ser Arg Glu Gln Ala Gly Lys Ala
 210 215 220
 Gly Leu Gly Thr Thr Phe Xaa Pro Asn Val Tyr Asp Phe Asp Tyr Met
 225 230 235 240
 Arg Arg Glu Ala Asn Gly Glu Ser Pro Lys Ser Ala Leu Ala Thr Glu
 245 250 255
 Val Ile Tyr Gly Asn Asn His Gly Lys Gln Ser Leu Asp Lys Thr Tyr
 260 265 270
 Leu Ala Ala Ala Leu Gly Thr Gly Lys Val Thr Ile Glu Thr Leu His
 275 280 285
 Gln Val Arg Ala Ile His Gln Gln Pro Asp Gly Ser Tyr Val Leu Ser
 290 295 300
 Val Asp Gln Ile Asp Thr Ala Gly Gln Thr Val Ala His Lys Glu Ile
 305 310 315 320
 Ser Cys Arg His Leu Phe Leu Gly Ala Gly Ser Leu Gly Ser Thr Glu
 325 330 335
 Leu Leu Val Arg Ala Arg Asp Thr Gly Ala Leu Pro Asp Leu Asn Ala
 340 345 350
 Glu Val Gly Ala Gly Trp Gly Pro Asn Gly Asn Ile Met Thr Gly Arg
 355 360 365
 Ala Asn His Val Trp Asn Pro Thr Gly Ala His Gln Ser Ser Ile Pro
 370 375 380
 Ala Leu Gly Ile Asp Asp Trp Asn Asn Pro Thr Ala Pro Val Xaa Ala
 385 390 395 400
 Glu Ile Ala Pro Met Pro Ala Gly Leu Glu Thr Trp Val Ser Leu Tyr
 405 410 415
 Leu Ala Ile Thr Lys Asn Pro Glu Arg Gly Thr Phe Val Tyr Asp Lys
 420 425 430
 Ala Thr Asp Arg Ala Ala Leu Arg Trp Thr Arg Asp Gln Asn Thr Pro
 435 440 445
 Ala Val Asn Ala Ala Arg Ser Leu Phe Asp Arg Ile Asn Lys Ala Asn
 450 455 460
 Gly Thr Met Tyr Arg Tyr Asp Leu Phe Gly Pro Gln Leu Lys Asn Phe
 465 470 475 480
 Ser Asp Asp Phe Cys Tyr His Pro Leu Gly Gly Cys Val Leu Gly Lys
 485 490 495
 Ala Thr Asp Gly Tyr Gly Arg Val Ala Gly Tyr His Asn Leu Tyr Val
 500 505 510
 Thr Asp Gly Ala Leu Ile Pro Gly Ser Ile Gly Val Asn Pro Phe Val
 515 520 525
 Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg Ile Ile Ala Glu
 530 535 540
 Asp Val Lys Ala Ala
 545

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<210> SEQ ID NO 5
<211> LENGTH: 552
<212> TYPE: PRT
<213> ORGANISM: Streptomyces chattanoogenensis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (165)..(165)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (234)..(234)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (402)..(402)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa165 is Met, then Xaa402 is not Phe

<400> SEQUENCE: 5

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Met Phe Asn Gln Gln Asn Gln His Leu Ser Arg Arg Arg Arg Leu Leu
 1 5 10 15

Gly Leu Ala Ala Leu Ser Gly Ala Ala Val Ala Gly Met Thr Thr Ile
 20 25 30

Ser Ala Ala Pro Arg Ala Ala Ala Asp Lys Arg Ser Pro Lys Ala
 35 40 45

Gly Ser Gly Ser Phe Val Pro Ala Val Val Ile Gly Thr Gly Tyr Gly
 50 55 60

Ala Ala Val Ser Ala Leu Arg Leu Gly Glu Ala Gly Ile Pro Thr Leu
 65 70 75 80

Met Leu Glu Met Gly Gln Leu Trp Asn Lys Pro Ala Asp Asp Gly Asn
 85 90 95

Val Phe Cys Gly Met Leu Lys Pro Asp Arg Arg Ser Ser Trp Phe Lys
 100 105 110

Ser Arg Thr Glu Ala Pro Leu Gly Ser Phe Leu Trp Leu Asp Val Ile
 115 120 125

Asn Arg Asp Ile Asp Pro Tyr Ala Gly Val Leu Asp Lys Val His Phe
 130 135 140

Asp Gln Met Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser Leu
 145 150 155 160

Val Asn Gly Gly Xaa Ala Val Val Pro Lys Arg Ser Tyr Phe Glu Glu
 165 170 175

Val Leu Pro Arg Val Asp Ala Ala Glu Met Tyr Asp Arg Tyr Phe Pro
 180 185 190

Arg Ala Asn Ser Met Leu Lys Val Asn His Ile Asp Lys Gly Trp Phe
 195 200 205

Glu Glu Thr Glu Trp Tyr Lys Phe Ala Arg Val Ser Arg Glu Gln Ala
 210 215 220

Gly Lys Ala Gly Leu Ser Thr Thr Phe Xaa Pro Asn Val Tyr Asp Phe
 225 230 235 240

Asp Tyr Met Arg Arg Glu Ala Asn Gly Glu Ser Pro Lys Ser Ala Leu
 245 250 255

Ala Thr Glu Val Ile Tyr Gly Asn Asn His Gly Lys Gln Ser Leu Asp
 260 265 270

Lys Thr Tyr Leu Ala Ala Leu Gly Thr Gly Lys Val Thr Ile Glu
 275 280 285

Thr Leu His Gln Val Lys Ala Ile His Gln Gln Pro Asp Gly Ser Tyr
 290 295 300

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Val Leu Ser Val Asp Gln Ile Asp Thr Ala Gly Gln Thr Val Ala His
305 310 315 320

Lys Glu Ile Ala Cys Arg His Leu Phe Leu Gly Ala Gly Ser Leu Gly
325 330 335

Ser Thr Glu Leu Leu Val Arg Ala Arg Asp Thr Gly Ala Leu Pro Asp
340 345 350

Leu Asn Ala Glu Val Gly Ala Gly Trp Gly Pro Asn Gly Asn Ile Met
355 360 365

Thr Gly Arg Ala Asn His Val Trp Asn Thr Thr Gly Ala His Gln Ser
370 375 380

Ser Ile Pro Ala Leu Gly Ile Asp Asp Trp Asp Asn Pro Ala Ala Pro
385 390 395 400

Val Xaa Ala Glu Ile Ala Pro Met Pro Ala Gly Leu Glu Thr Trp Val
405 410 415

Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Gly Thr Phe Val
420 425 430

Tyr Asp Lys Ala Thr Asp Arg Ala Ala Leu Arg Trp Thr Arg Asp Gln
435 440 445

Asn Thr Pro Ala Val Asn Ala Ala Lys Ser Leu Phe Asp Arg Ile Asn
450 455 460

Lys Ala Asn Thr Thr Met Tyr Arg Tyr Asp Leu Phe Gly Pro Gln Leu
465 470 475 480

Lys Asn Phe Ser Asp Asp Phe Cys Tyr His Pro Leu Gly Gly Cys Val
485 490 495

Leu Gly Lys Ala Thr Asp Gly Tyr Gly Arg Val Ala Gly Tyr Arg Asn
500 505 510

Leu Tyr Val Thr Asp Gly Ala Leu Ile Pro Gly Ser Ile Gly Val Asn
515 520 525

Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg Ile
530 535 540

Ile Ala Glu Asp Val Lys Ala Ala
545 550

<210> SEQ_ID NO 6
<211> LENGTH: 549
<212> TYPE: PRT
<213> ORGANISM: Streptomyces diastaticus
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (162)..(162)
<223> OTHER_INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (231)..(231)
<223> OTHER_INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (399)..(399)
<223> OTHER_INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa162 is Met, then Xaa399 is not Phe
<400> SEQUENCE: 6

Met Ile Glu Asn Gln His Leu Ser Arg Arg Arg Leu Leu Gly Leu Ala
1 5 10 15

Ala Leu Gly Gly Ala Ala Val Ala Gly Met Thr Thr Ile Ser Val Ala
20 25 30

Pro Arg Ala Ala Ala Ala Gly Gln Gly Ser Pro Arg Ala Gly Asp Gly

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35	40	45
Ala Phe Val Pro Ala Val Val Ile Gly Thr Gly Tyr Gly Ala Ala Val		
50	55	60
Ser Ala Leu Arg Leu Gly Glu Ala Gly Ile Pro Thr Leu Met Leu Glu		
65	70	75
Met Gly Gln Leu Trp Asn Lys Pro Ala Asp Asp Gly Asn Ile Phe Cys		
85	90	95
Gly Met Leu Lys Pro Asp Arg Arg Ser Ser Trp Phe Lys Ser Arg Thr		
100	105	110
Glu Ala Pro Leu Gly Ser Phe Leu Trp Leu Asp Val Ile Asn Arg Asn		
115	120	125
Ile Asp Pro Tyr Ala Gly Val Leu Asp Lys Val His Phe Asp Glu Met		
130	135	140
Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly		
145	150	155
160		
Gly Xaa Ala Val Val Pro Lys Arg Ser Tyr Phe Glu Glu Val Leu Pro		
165	170	175
Arg Val Asp Ala Ala Gln Met Tyr Asp Arg Tyr Phe Pro Arg Ala Asn		
180	185	190
Ser Met Leu Lys Val Asn His Ile Asp Lys Gly Trp Phe Glu Asp Thr		
195	200	205
Glu Trp Tyr Lys Tyr Ala Arg Val Ser Arg Glu Gln Ala Gly Lys Ala		
210	215	220
Gly Leu Ser Thr Thr Phe Xaa Pro Asn Val Tyr Asp Phe Asp His Met		
225	230	235
240		
Arg Arg Glu Ala Asp Gly Thr Ala Pro Lys Ser Ala Leu Ala Gly Glu		
245	250	255
Val Ile Tyr Gly Asn Asn His Gly Lys Gln Ser Leu Asp Lys Thr Tyr		
260	265	270
Leu Ala Ala Ala Leu Gly Thr Gly Lys Val Thr Ile Glu Thr Leu His		
275	280	285
Gln Val Lys Ala Ile Arg Arg Gln Pro Asp Gly Ser Tyr Val Leu Ser		
290	295	300
Val Val Gln Ser Asp Ala Asp Gly Lys Thr Ile Ala Gln Lys Glu Ile		
305	310	315
320		
Gly Cys Arg His Leu Phe Leu Gly Ala Gly Ser Leu Gly Ser Thr Glu		
325	330	335
Leu Leu Val Arg Ala Arg Asp Thr Gly Thr Leu Pro Glu Leu Asn Ala		
340	345	350
Glu Val Gly Ala Gly Trp Gly Pro Asn Gly Asn Ile Met Thr Gly Arg		
355	360	365
Ala Asn His Val Trp Asn Pro Thr Gly Ala His Gln Ser Ser Ile Pro		
370	375	380
Ala Leu Gly Ile Asp Asp Trp Asp Asn Pro Ala Ala Pro Val Xaa Ala		
385	390	395
400		
Glu Ile Ala Pro Met Pro Ala Gly Leu Glu Thr Trp Val Ser Leu Tyr		
405	410	415
Leu Ala Ile Thr Lys Asn Pro Glu Arg Gly Thr Phe Val Tyr Asp Lys		
420	425	430
Ala Thr Asp Arg Ala Lys Leu Arg Trp Thr Arg Asp Gln Asn Thr Pro		
435	440	445
Ala Val Asn Ala Ala Lys Ser Leu Phe Asp Arg Ile Asn Lys Ala Asn		
450	455	460

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Thr Thr Met Tyr Arg Tyr Asp Leu Phe Gly Ser Gln Leu Lys Asn Phe
 465 470 475 480

Ser Asp Asp Phe Ser Tyr His Pro Leu Gly Gly Cys Val Leu Gly Lys
 485 490 495

Ala Thr Asp Leu Tyr Gly Arg Val Ala Gly Tyr Gln Asn Leu Tyr Val
 500 505 510

Met Asp Gly Ala Leu Val Pro Gly Ser Ile Gly Val Asn Pro Phe Val
 515 520 525

Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg Ile Ile Ala Glu
 530 535 540

Asp Val Lys Ala Ala
 545

<210> SEQ ID NO 7
<211> LENGTH: 552
<212> TYPE: PRT
<213> ORGANISM: Streptomyces griseus
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (165)..(165)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
 Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (234)..(234)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (402)..(402)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa165 is Met, then Xaa402 is not Phe

<400> SEQUENCE: 7

Met Phe Glu Asn Gln Gln Asn Gln His Leu Ser Arg Arg Arg Leu Leu
 1 5 10 15

Gly Leu Ala Ala Leu Ser Gly Ala Ala Val Ala Gly Leu Thr Thr Ile
 20 25 30

Ser Ala Ala Pro Gln Ala Ala Ala Gly Arg Arg Ala Pro Arg Ala
 35 40 45

Gly Asp Gly Ser Phe Val Glu Ala Val Val Ile Gly Thr Gly Tyr Gly
 50 55 60

Ala Ala Val Ser Ala Leu Arg Leu Gly Glu Ala Gly Val Pro Thr Leu
 65 70 75 80

Met Leu Glu Met Gly Arg Leu Trp Asn Lys Pro Ala Glu Asp Gly Asn
 85 90 95

Ile Phe Cys Gly Met Leu Lys Pro Asp Arg Arg Ser Thr Trp Phe Lys
 100 105 110

Ser Arg Thr Glu Ala Pro Leu Gly Ser Phe Leu Trp Leu Asp Val Val
 115 120 125

Asn Arg Asp Ile Asp Pro Tyr Ala Gly Val Leu Asp Arg Val His Phe
 130 135 140

Asp Glu Met Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser Leu
 145 150 155 160

Val Asn Gly Gly Xaa Ala Val Val Pro Lys Arg Ala Tyr Phe Glu Glu
 165 170 175

Val Leu Pro Lys Val Asp Ala Ala Glu Met Tyr Asp Arg Tyr Phe Pro
 180 185 190

Arg Ala Asn Ser Met Leu Lys Val Asn His Ile Asp Lys Thr Trp Phe

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195	200	205
Glu Asp Thr Glu Trp Tyr Lys Phe Ala Arg Val Ser Arg Glu Gln Ala		
210	215	220
Ser Lys Ala Gly Leu Gly Thr Thr Phe Xaa Pro Asn Val Tyr Asp Phe		
225	230	235 240
Gly His Met Arg Arg Glu Ala Thr Gly Glu Ala Pro Lys Ser Ala Leu		
245	250	255
Ala Gly Glu Val Ile Tyr Gly Asn Asn His Gly Lys Gln Ser Leu Asp		
260	265	270
Lys Thr Tyr Leu Ala Ala Leu Gly Thr Gly Lys Val Thr Ile Glu		
275	280	285
Thr Leu His Gln Val Lys Ala Ile Arg Gln Gln Lys Asp Gly Gly Tyr		
290	295	300
Val Leu Ser Val Asp Gln Thr Asp Ala Asp Gly Lys Thr Val Gly His		
305	310	315 320
Lys Glu Ile Gly Cys Arg His Leu Phe Leu Gly Ala Gly Ser Leu Gly		
325	330	335
Ser Thr Glu Leu Leu Val Arg Ala Arg Asp Thr Gly Ala Leu Pro Asp		
340	345	350
Leu Asn Ala Glu Val Gly Gly Trp Gly Pro Asn Gly Asn Ile Met		
355	360	365
Thr Gly Arg Ala Asn His Val Trp Asn Pro Thr Gly Ala His Gln Ser		
370	375	380
Ser Ile Pro Ala Leu Gly Ile Asp Asp Trp Asn Asn Ala Ala Ala Pro		
385	390	395 400
Val Xaa Ala Glu Ile Ala Pro Met Pro Ala Gly Ala Glu Thr Trp Val		
405	410	415
Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Gly Thr Phe Val		
420	425	430
Tyr Asp Lys Ala Thr Asp Arg Val Ala Leu Arg Trp Thr Arg Asp Gln		
435	440	445
Asn Thr Pro Ala Val Asn Ala Ala Lys Ser Leu Phe Asp Arg Ile Asn		
450	455	460
Gln Ala Asn Thr Thr Val Tyr Arg Tyr Asp Leu Phe Gly Lys Gln Val		
465	470	475 480
Lys Ala Phe Ser Asp Asp Phe Ser Tyr His Pro Leu Gly Gly Cys Val		
485	490	495
Leu Gly Lys Ala Thr Asp Leu Tyr Gly Arg Val Ala Gly His Arg Asn		
500	505	510
Leu Tyr Val Met Asp Gly Ser Leu Ile Pro Gly Ser Ile Gly Val Asn		
515	520	525
Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg Ile		
530	535	540
Ile Ala Glu Asp Val Lys Ala Ala		
545	550	

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<210> SEQ_ID NO 8
<211> LENGTH: 547
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp.
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (160)...(160)
<223> OTHER_INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:

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<221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (229)..(229)
 <223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (397)..(397)
 <223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa160 is Met, then Xaa397 is not Phe

<400> SEQUENCE: 8

Met	Asn	Ala	His	Gln	Pro	Leu	Ser	Arg	Arg	Arg	Met	Leu	Gly	Leu	Ala
1															
												10		15	

Ala	Leu	Gly	Ala	Ala	Ala	Leu	Thr	Gly	Gln	Thr	Thr	Ile	Thr	Ala	Ala
												20		25	30

Pro	Arg	Ala	Ala	Ala	Ala	Ala	Thr	Ala	Pro	Gly	Gly	Ser	Gly	Gly	Thr	Phe
												35		40	45	

Val	Pro	Ala	Val	Val	Ile	Gly	Thr	Gly	Tyr	Gly	Ala	Ala	Val	Ser	Ala
												50		55	60

Leu	Arg	Leu	Gly	Glu	Ala	Gly	Val	Ser	Thr	Leu	Met	Leu	Glu	Met	Gly	
												65		70	75	80

Gln	Leu	Trp	Asn	Gln	Pro	Gly	Pro	Asp	Gly	Asn	Val	Phe	Cys	Gly	Met
												85		90	95

Leu	Lys	Pro	Asp	Lys	Arg	Ser	Ser	Trp	Phe	Lys	Thr	Arg	Thr	Glu	Ala
												100		105	110

Pro	Leu	Gly	Ser	Phe	Leu	Trp	Leu	Asp	Leu	Ala	Asn	Arg	Asp	Ile	Asp
												115		120	125

Pro	Tyr	Ala	Gly	Val	Leu	Asp	Arg	Val	Asn	Phe	Asp	Gln	Met	Ser	Val
												130		135	140

Tyr	Val	Gly	Arg	Gly	Val	Gly	Gly	Ser	Leu	Val	Asn	Gly	Gly	Xaa		
												145		150	155	160

Ala	Val	Thr	Pro	Arg	Arg	Ser	Ser	Tyr	Phe	Gln	Glu	Val	Leu	Pro	Gln	Val
												165		170	175	

Asp	Ala	Asp	Glu	Met	Tyr	Gly	Thr	Tyr	Phe	Pro	Arg	Ala	Asn	Ser	Gly
												180		185	190

Leu	Arg	Val	Asn	Asn	Ile	Asp	Lys	Asp	Trp	Phe	Glu	Gln	Thr	Glu	Trp
												195		200	205

Tyr	Thr	Phe	Ala	Arg	Val	Ala	Arg	Leu	Gln	Ala	Glu	Asn	Ala	Gly	Leu
												210		215	220

Lys	Thr	Thr	Phe	Xaa	Pro	Asn	Val	Tyr	Asp	Trp	Asp	Tyr	Met	Arg	Gly	
												225		230	235	240

Glu	Ala	Asp	Gly	Thr	Asn	Pro	Lys	Ser	Ala	Leu	Ala	Glu	Val	Ile	
												245		250	255

Tyr	Gly	Asn	Asn	His	Gly	Lys	Val	Ser	Leu	Asp	Lys	Ser	Tyr	Leu	Ala
												260		265	270

Ala	Ala	Leu	Gly	Thr	Gly	Lys	Val	Thr	Val	Glu	Thr	Leu	His	Gln	Val
												275		280	285

Lys	Thr	Ile	Arg	Gln	Gln	Asn	Asn	Gly	Thr	Tyr	Leu	Leu	Thr	Val	Glu
												290		295	300

Gln	Lys	Asp	Pro	Asp	Gly	Lys	Leu	Leu	Gly	Thr	Lys	Glu	Ile	Ser	Cys	
												305		310	315	320

Arg	His	Leu	Phe	Leu	Gly	Ala	Gly	Ser	Leu	Gly	Ser	Ile	Glu	Leu	Leu
												325		330	335

Leu	Arg	Ala	Arg	Glu	Thr	Gly	Thr	Leu	Pro	Gly	Leu	Ser	Ser	Glu	Ile
												340		345	350

Gly Gly Gly Trp Gly Pro Asn Gly Asn Ile Met Thr Ala Arg Ala Asn

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355	360	365
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His Val Trp Asn Pro Thr Gly Ser Lys Gln Ser Ser Ile Pro Ala Leu		
370	375	380

Gly Ile Asp Asp Trp Asp Asn Pro Asp Asn Pro Val Xaa Ala Glu Ile		
385	390	395
		400

Ala Pro Met Pro Ala Gly Leu Glu Thr Trp Val Ser Leu Tyr Leu Ala		
405	410	415

Ile Thr Lys Asn Pro Glu Arg Gly Thr Phe Val Tyr Asp Ala Ala Lys		
420	425	430

Asp Arg Ala Asp Leu Arg Trp Thr Arg Asp Gln Asn Ala Pro Ala Val		
435	440	445

Ala Ala Ala Lys Ser Leu Phe Asp Arg Val Asn Lys Ala Asn Thr Thr		
450	455	460

Ile Tyr Arg Tyr Asp Leu Phe Gly Lys Gln Ile Lys Ala Phe Ala Asp		
465	470	475
		480

Asp Phe Cys Tyr His Pro Leu Gly Gly Cys Val Leu Gly Lys Ala Thr		
485	490	495

Asp Asn Tyr Gly Arg Val Ser Gly Tyr Lys Asn Leu Tyr Val Thr Asp		
500	505	510

Gly Ser Leu Ile Pro Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile		
515	520	525

Thr Ala Leu Ala Glu Arg Asn Val Glu Arg Val Ile Lys Glu Asp Ile		
530	535	540

Ala Gly Ser
545

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<210> SEQ_ID NO 9
<211> LENGTH: 543
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp.
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (157) ..(157)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (226) ..(226)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (394) ..(394)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa157 is Met, then Xaa394 is not Phe

<400> SEQUENCE: 9

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Met Pro Gly Met Ala Ser Leu Asn Arg Arg Arg Phe Leu Gly Leu Ala		
1	5	10
		15

Ala Leu Asn Ser Ala Ala Leu Gly Leu Thr Ser Ile Ser Ala Thr		
20	25	30

Thr Ala Arg Ala Ala Thr Val Ala Pro Leu Pro Asp Tyr Ser Pro Ala		
35	40	45

Val Val Ile Gly Thr Gly Tyr Gly Ala Ala Val Thr Ala Leu Arg Leu		
50	55	60

Gly Glu Ala Gly Val Pro Thr Val Met Leu Glu Met Gly Gln Leu Trp		
65	70	75
		80

Asn Glu Ala Gly Pro Asp Gly Lys Val Phe Cys Asp Met Leu Lys Pro		
85	90	95

-continued

Asp Arg Arg Ser Met Trp Phe Lys Lys Arg Thr Glu Ala Pro Leu Ala
100 105 110

Ser Phe Leu Trp Leu Asp Val Ala Asn His Asp Ile Asp Pro Tyr Ala
115 120 125

Gly Val Leu Asp Arg Val Asn Tyr Gly Gly Met Ser Val Tyr Val Gly
130 135 140

Arg Gly Val Gly Gly Ser Leu Val Asn Gly Ala Xaa Ala Val Gln
145 150 155 160

Pro Lys Arg Ser Tyr Phe Glu Glu Ile Leu Pro Arg Val Asp Ala Asp
165 170 175

Glu Met Tyr Gly Lys Tyr Tyr Pro Arg Ala Asn Ala Gly Leu Gly Val
180 185 190

Asn His Ile Asp Pro Asp Trp Phe Glu Thr Cys Lys Ser Tyr Gln Phe
195 200 205

Ala Arg Val Ser Arg Lys Ala Ala Gln Lys Thr Gly Leu Lys Thr Thr
210 215 220

Phe Xaa Pro Ser Val Tyr Asp Phe Glu Tyr Met Lys Lys Glu Glu Ala
225 230 235 240

Gly Thr Val Glu Arg Ser Ala Leu Ala Ser Glu Val Ile Tyr Gly Asn
245 250 255

Asn His Gly Lys Arg Ser Leu Asp Lys Thr Tyr Leu Ala Ala Leu
260 265 270

Gly Thr Gly His Val Thr Ile Gln Thr Leu His Glu Val Arg Glu Ile
275 280 285

Ile Gln Gln Gln Asp Gly Thr Tyr Thr Leu Val Val Arg Glu Ser Asp
290 295 300

Ala Leu Gly Asn Val Leu Ala Thr Lys His Leu Ser Thr Lys Tyr Leu
305 310 315 320

Phe Leu Gly Ala Gly Ser Leu Gly Ser Thr Glu Leu Leu Val Arg Ala
325 330 335

Arg Asp Thr Gly Arg Leu Pro Arg Leu Ser Glu Ala Val Gly Gln Gly
340 345 350

Trp Gly Thr Asn Gly Asn Val Met Leu Gly Arg Ala Asn His Val Trp
355 360 365

Asp Thr Thr Gly Ser Leu Glu Ser Gly Met Pro Ala Leu Gly Ile Asp
370 375 380

Asp Trp Asp Asn Pro Ala His Pro Val Xaa Ala Glu Ile Ala Pro Val
385 390 395 400

Pro Ala Gly Leu Glu Thr Trp Ala Ser Leu Tyr Leu Ala Ile Thr Lys
405 410 415

Asn Pro Glu Arg Gly His Phe Thr Tyr Asp Ala Ala Ser Asp Ser Ala
420 425 430

Lys Leu Gln Trp Ser Pro Asp Gln Gly Gln Pro Ser Ile Asp Ala Ala
435 440 445

Lys Ser Leu Phe Asp Arg Ile Asn Lys Ala Asn Ser Thr Ile Tyr Arg
450 455 460

Tyr Asp Leu Phe Gly Asp Thr Arg Ala Phe Glu Asn Arg Phe Thr Tyr
465 470 475 480

His Pro Leu Gly Gly Leu Val Leu Gly Glu Ala Thr Asp Asp Tyr Gly
485 490 495

Arg Val Lys Gly Tyr Arg Asn Leu Tyr Val Thr Asp Gly Ser Leu Ile
500 505 510

Pro Gly Ser Thr Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala

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515

520

525

Glu Arg Asn Ile Glu Arg Val Leu Ala Glu Asp Gly Val Arg Ala
 530 535 540

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<210> SEQ_ID NO 10
<211> LENGTH: 547
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp.
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (165) ..(165)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
  Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (234) ..(234)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
  Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (402) ..(402)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
  or Asp, provided that when Xaa165 is Met, then Xaa402 is not Phe

<400> SEQUENCE: 10

Met Ala Gly Trp Ala Glu Ser Ala His Asp Ala Ala Met Thr His Asn
  1           5           10          15

Leu Thr Arg Arg Gln Leu Gly Leu Asn Ala Leu Arg Ala Ala Ala Ala
  20          25          30

Leu Gly Ile Thr Arg Ile Gly Leu Gly Ala Ala Ala Ala Ala Glu Pro
  35          40          45

Pro Ala Ala Pro Tyr Ala Pro Ala Val Val Val Gly Ser Gly Tyr Gly
  50          55          60

Ser Ala Val Ala Ala Leu Arg Leu Gly Gln Ala Gly Val Arg Thr Val
  65          70          75          80

Val Leu Glu Met Gly Arg Leu Trp Asp Thr Pro Gly Pro Asp Gly Lys
  85          90          95

Val Phe Pro Ser Thr Ser Ala Pro Asp Gln Arg Ser Met Trp Phe Arg
  100         105         110

Thr Arg Thr Glu Ala Pro Leu Ala Gln Phe Leu Trp Leu Asp Val Val
  115         120         125

Asn Arg Asp Ile Ser Pro Tyr Pro Gly Val Leu Asp Arg Val Asn His
  130         135         140

Gly Gly Met Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser Leu
  145         150         155         160

Val Asn Gly Gly Xaa Ala Pro Thr Pro Arg Arg Ser Tyr Phe Ala Glu
  165         170         175

Val Phe Pro Arg Val Asp Ala Glu Glu Met Tyr Gly Thr Tyr Phe Pro
  180         185         190

Arg Ala Arg Ala Met Leu Gly Val Asn Gly Ile Asp Pro Ala Trp Phe
  195         200         205

Glu Ser Thr Glu Trp Tyr Arg Phe Ala Arg Ile Ser Arg Lys His Ala
  210         215         220

Gln Asn Thr Gly Leu Lys Thr Thr Phe Xaa Pro Asn Val Tyr Asp Phe
  225         230         235         240

Gly Tyr Met Lys Arg Glu Ala Ala Gly Thr Ala Thr Arg Ser Ala Leu
  245         250         255

Ala Gly Glu Val Ile Tyr Gly Asn Asn His Gly Lys Lys Ser Val Asp
  260         265         270

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Lys Thr Tyr Leu Ala Ala Ala Leu Gly Thr Gly Asn Val Thr Ile Glu
275 280 285

Thr Met Gln Arg Val Val Ala Val Arg Gln Asp Leu Ala Gly Gly Tyr
290 295 300

Val Leu Thr Val His Thr Ser Asp Val Thr Gly Arg Val Thr Gln Val
305 310 315 320

Arg Glu Leu Gly Cys Arg Gln Leu Phe Leu Gly Ala Gly Ser Leu Gly
325 330 335

Thr Thr Glu Ile Leu Leu Arg Ala Arg Glu Thr Gly Ala Leu Pro Ala
340 345 350

Leu Ser Glu Lys Val Gly Leu Gly Trp Gly Pro Asn Gly Asn Val Met
355 360 365

Thr Ala Arg Ala Asn His Leu Trp Asp Thr Val Gly Cys Asn Gln Ala
370 375 380

Thr Met Pro Ala Leu Gly Ile Asp Asp Trp Asp Asn Ala Ala Asn Pro
385 390 395 400

Val Xaa Ala Glu Ile Ala Pro Leu Pro Met Gly Ile Glu His Trp Ile
405 410 415

Ser Met Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Gly Arg Phe Val
420 425 430

Tyr Asp Ala Ala Thr Asp Ser Ala Arg Leu Asn Trp Thr Arg Asp Gln
435 440 445

Asn Ala Pro Ala Val Ala Ala Lys Asn Leu Phe Asp Arg Ile Asn
450 455 460

Arg Arg Asn Val Thr Ile Tyr Arg Tyr Asp Leu Phe Gly Asp Asn Lys
465 470 475 480

Ala Phe Ala Asp Asp Phe Thr Tyr His Pro Leu Gly Gly Cys Val Leu
485 490 495

Gly Glu Ala Thr Asp Ala Tyr Gly Arg Val Lys Gly Tyr Gln Gly Leu
500 505 510

Tyr Val Leu Asp Gly Ser Leu Val Pro Gly Ser Leu Gly Val Asn Pro
515 520 525

Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Met Glu Arg Ile Leu
530 535 540

Ala Gln Pro
545

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<210> SEQ_ID NO 11
<211> LENGTH: 550
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp.
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (166)..(166)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (235)..(235)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (403)..(403)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa166 is Met, then Xaa403 is not Phe

<400> SEQUENCE: 11

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Met Gly Gly Arg Arg Glu Ser Ala His Asp Ala Ala Met Thr Ser Asn
1 5 10 15

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Leu Thr Arg Arg Gln Met Leu Gly Leu Gly Ala Leu Ser Thr Ala Ala
 20 25 30
 Ala Leu Gly Phe Thr Arg Ile Gly Ala Ala Ser Ala Ala Leu Glu
 35 40 45
 Pro Pro Ala Ala Ser Tyr Ala Pro Ala Ile Val Val Gly Ser Gly Tyr
 50 55 60
 Gly Ser Ala Val Ala Ala Leu Arg Leu Gly Gln Ala Gly Val Arg Thr
 65 70 75 80
 Val Val Leu Glu Met Gly Arg Leu Trp Asp Thr Pro Gly Ala Asp Gly
 85 90 95
 Lys Val Phe Pro Ser Thr Ser Ala Pro Asp Gln Arg Ser Met Trp Phe
 100 105 110
 Arg Asn Arg Thr Glu Ala Pro Leu Ala Gln Phe Leu Trp Leu Asp Val
 115 120 125
 Val Asn Arg Asp Ile Ser Pro Tyr Pro Gly Val Leu Asp Arg Val Asn
 130 135 140
 Tyr Gly Asp Met Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser
 145 150 155 160
 Leu Val Asn Gly Gly Xaa Ser Pro Thr Pro Arg Arg Ser Tyr Phe Ser
 165 170 175
 Glu Val Leu Pro Arg Val Asp Ala Asp Glu Met Tyr Gly Thr Tyr Tyr
 180 185 190
 Pro Arg Ala Arg Ala Met Leu Gly Val Gly Asp Ile Asp Pro Ala Trp
 195 200 205
 Phe Glu Ser Thr Glu Trp Tyr Arg Phe Ala Arg Ile Ser Arg Lys His
 210 215 220
 Ala Gln Asn Thr Gly Leu Lys Thr Val Phe Xaa Pro Asn Val Tyr Asp
 225 230 235 240
 Phe Glu Tyr Met Lys Arg Glu Ala Ala Gly Thr Ala Thr Arg Ser Ala
 245 250 255
 Leu Ala Gly Glu Val Ile Tyr Gly Asn Asn His Gly Lys Ser Val
 260 265 270
 Asp Lys Thr Tyr Leu Ala Ala Ile Gly Thr Gly Asn Val Thr Ile
 275 280 285
 Glu Thr Met Gln Arg Val Val Ala Val Arg Gln Asp Pro Ala Gly Gly
 290 295 300
 Tyr Val Leu Thr Val Arg Thr Ser Asp Val Thr Gly Arg Val Thr Gln
 305 310 315 320
 Val Arg Glu Leu Gly Cys Arg Arg Leu Phe Leu Gly Ala Gly Ser Leu
 325 330 335
 Gly Thr Thr Glu Ile Leu Leu Arg Ala Arg Glu Thr Gly Thr Leu Pro
 340 345 350
 Ala Leu Ser Glu Lys Val Gly Leu Gly Trp Gly Pro Asn Gly Asn Val
 355 360 365
 Met Thr Ala Arg Ala Asn His Leu Trp Asp Thr Val Gly Ser Asn Gln
 370 375 380
 Ala Thr Met Pro Ala Leu Gly Ile Asp Asp Trp Asp Asn Ala Ala Asn
 385 390 395 400
 Pro Val Xaa Ala Glu Ile Ala Pro Leu Pro Met Gly Phe Glu His Trp
 405 410 415
 Ile Ser Met Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Gly His Phe
 420 425 430

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Thr Tyr Asp Ala Ala Ser Asp Ser Ala Arg Leu Gln Trp Arg Arg Asp
 435 440 445

Gln Asn Thr Pro Ala Val Arg Ala Ala Lys Asn Leu Phe Asp Arg Ile
 450 455 460

Asn Arg Ala Asn Phe Thr Ile Tyr Arg Tyr Asp Leu Phe Gly Gly Asn
 465 470 475 480

Lys Asn Phe Ala Asp Asp Phe Thr Tyr His Pro Leu Gly Gly Cys Val
 485 490 495

Leu Gly Glu Ala Thr Asp Asp Phe Gly Arg Ala Lys Gly Tyr Gln Gly
 500 505 510

Leu Tyr Val Val Asp Gly Ser Leu Val Pro Gly Ser Leu Gly Val Asn
 515 520 525

Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Met Ala Arg Ile
 530 535 540

Leu Ala Gln Asp Pro His
 545 550

<210> SEQ ID NO 12

<211> LENGTH: 540

<212> TYPE: PRT

<213> ORGANISM: Streptomyces scabiei

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (154)..(154)

<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
 Tyr, Lys or Ser

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (223)..(223)

<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (391)..(391)

<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa154 is Met, then Xaa391 is not Phe

<400> SEQUENCE: 12

Met Gln Arg Gln Leu Thr Arg Arg His Ile Leu Gly Met Ala Ala Leu
 1 5 10 15

Gln Thr Ala Ala Gly Leu Gly Leu Thr Arg Ile Gly Leu Gln Ser Ala
 20 25 30

Arg Ala Ala Glu Pro Asp Ala Val Asp Asn Ala Pro Ala Leu Val Ile
 35 40 45

Gly Ser Gly Tyr Gly Ala Ala Val Ala Ala Leu Arg Leu Gly Gln Ala
 50 55 60

Gly Ile Arg Thr Leu Val Leu Glu Met Gly Arg Ala Trp Thr Thr Pro
 65 70 75 80

Gly Ala Asp Gly Lys Ile Phe Cys Ser Thr Lys Glu Pro Asp Glu Arg
 85 90 95

Ser Met Trp Phe Lys Thr Arg Thr Glu Ala Pro Leu Ala Thr Phe Leu
 100 105 110

Trp Leu Asp Val Val Asn Gln Asp Ile Ser Arg Tyr Pro Gly Val Leu
 115 120 125

Asp Arg Val Arg His Ala Asn Met Ser Val Phe Leu Gly Arg Gly Val
 130 135 140

Gly Gly Gly Ser Leu Val Asn Gly Ser Xaa Ala Val Thr Pro Leu Arg
 145 150 155 160

Ser Tyr Phe Ala Glu Gln Phe Pro Thr Val Asp Thr Ala Glu Met Tyr
 165 170 175

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Ser Thr Tyr Phe Pro Arg Ala Arg Ser Met Leu Gly Val Asn Thr Val
180 185 190

Asp Pro Ala Trp Phe Glu Ser Thr Glu Trp Tyr Arg Phe Ser Arg Val
195 200 205

Ser Arg Ala His Ala Ala Lys Ala Gly Leu Arg Thr Thr Phe Xaa Pro
210 215 220

Ser Val Tyr Asp Phe Asp His Met Gln Arg Glu Ala Ala Gly Thr Ala
225 230 235 240

Thr Lys Ser Ala Leu Ala Gly Glu Val Ile Tyr Gly Asn Asn His Gly
245 250 255

Lys Lys Ser Leu Asp Lys Thr Tyr Leu Ala Ala Leu Gly Thr Gly
260 265 270

Asn Val Thr Ile His Thr Met Glu Arg Ala Arg Gly Ile Arg Arg Leu
275 280 285

Gly Asp Gly Thr Tyr Val Val Thr Ala Asp Arg Ile Asp Gly Thr Gly
290 295 300

Ala Val Val Glu Thr Lys Glu Tyr Gly Cys Thr Tyr Leu Phe Leu Gly
305 310 315 320

Ala Gly Ser Val Gly Thr Thr Glu Leu Leu Val Arg Ala Arg Ala Lys
325 330 335

Gly Thr Leu Pro Ala Leu Asn Ala Ser Val Gly Ala Gly Trp Gly Pro
340 345 350

Asn Gly Asn Val Met Leu Gly Arg Ala Asn His Leu Trp Asp Thr Val
355 360 365

Gly Ala Asn Gln Ser Thr Met Pro Val Met Gly Ile Asp Asp Trp Ala
370 375 380

Asn Thr Ala Asn Pro Val Xaa Ala Glu Ile Ala Pro Leu Pro Thr Gly
385 390 395 400

Leu Glu His Trp Val Ser Leu Tyr Leu Ala Ile Thr Lys Asn Thr Glu
405 410 415

Arg Ala Ser Phe Thr Tyr Asp Ala Ala Thr Asp Ser Ala Lys Leu Gly
420 425 430

Trp Ser Ala Ala Gln Ser Ala Val Ser Ser Ser Met Ala Lys Lys Leu
435 440 445

Phe Asp Arg Ile Asn Ser Ala Asn Ser Thr Met Tyr Arg Tyr Asp Leu
450 455 460

Phe Gly Ser Ser Asn Lys Val Phe Ala Asp Asp Phe Thr Tyr His Pro
465 470 475 480

Leu Gly Gly Cys Val Leu Gly Arg Ala Thr Asp Asp Tyr Gly Arg Val
485 490 495

Lys Gly Tyr Glu Asn Leu Tyr Val Thr Asp Gly Ser Leu Val Pro Gly
500 505 510

Ser Ile Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg
515 520 525

Asn Val Ala Arg Val Leu Val Glu Asp Thr Ala Pro
530 535 540

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<210> SEQ_ID NO 13
<211> LENGTH: 543
<212> TYPE: PRT
<213> ORGANISM: Streptomyces bingchenggensis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (158) ..(158)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,

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Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (227) .. (227)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (395) .. (395)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa158 is Met, then Xaa395 is not Phe

<400> SEQUENCE: 13

Met	Thr	Ala	Asn	Leu	Thr	Arg	Arg	His	Ile	Leu	Gly	Leu	Ala	Ala	Leu
1				5					10				15		
Arg	Gly	Ala	Ala	Ala	Leu	Gly	Leu	Thr	Arg	Ile	Ala	Leu	Ser	Pro	Ala
		20				25				30					
Ala	Ala	Ala	Asp	Arg	Pro	Ala	Pro	Ala	Ala	Ser	Ala	Glu	Tyr	Ala	Pro
			35			40				45					
Ala	Val	Val	Val	Gly	Ser	Gly	Tyr	Gly	Ala	Ala	Val	Ala	Ala	Leu	Arg
			50			55				60					
Leu	Gly	Glu	Ala	Gly	Val	Lys	Thr	Leu	Val	Leu	Glu	Met	Gly	Arg	Leu
		65			70			75			80				
Trp	Asn	Ala	Pro	Ala	Ser	Asp	Gly	Lys	Val	Tyr	Cys	Ser	Met	Thr	Ala
			85			90			95						
Pro	Asp	Arg	Arg	Ser	Met	Trp	Phe	Lys	Thr	Arg	Thr	Glu	Ala	Pro	Leu
			100			105			110						
Ala	Thr	Phe	Leu	Trp	Leu	Asp	Val	Ile	Asn	Lys	Asp	Ile	Thr	Pro	Tyr
			115			120			125						
Pro	Gly	Val	Leu	Asp	Arg	Val	Arg	Phe	Pro	Asn	Met	Ser	Val	Tyr	Val
		130			135			140							
Gly	Arg	Gly	Val	Gly	Gly	Ser	Leu	Val	Asn	Gly	Gly	Xaa	Ala	Val	
	145			150			155			160					
Thr	Pro	Ser	Arg	Ala	Tyr	Phe	Gln	Glu	Val	Leu	Pro	Gln	Val	Asp	Ala
			165			170			175						
Asp	Ala	Met	Tyr	Ala	Thr	Tyr	Phe	Pro	Leu	Ala	Asn	Arg	Met	Leu	Gly
			180			185			190						
Ala	Ala	Thr	Val	Pro	Ser	Ala	Trp	Phe	Glu	Ser	Thr	Glu	Trp	Tyr	Lys
			195			200			205						
Tyr	Ala	Arg	Val	Ser	Arg	Asp	Gln	Ala	Lys	Thr	Ala	Gly	Leu	Lys	Thr
			210			215			220						
Val	Phe	Xaa	Pro	Asn	Val	Tyr	Asp	Phe	Asp	Tyr	Met	Gln	Arg	Glu	Ala
		225			230			235			240				
Ala	Gly	Thr	Ala	Thr	Lys	Ser	Ala	Leu	Ala	Gln	Glu	Val	Ile	Tyr	Gly
			245			250			255						
Asn	Asn	Phe	Gly	Lys	Arg	Ser	Leu	Asp	Lys	Thr	Tyr	Leu	Ala	Ala	
			260			265			270						
Leu	Gly	Thr	Gly	Asn	Val	Thr	Ile	Arg	Thr	Leu	Ser	Arg	Ala	Arg	Ala
			275			280			285						
Ile	Arg	Arg	Ala	Ala	Asp	Gly	Thr	Tyr	Val	Leu	Thr	Val	Asp	Arg	Leu
			290			295			300						
Asp	Asp	Thr	Gly	Ala	Val	Val	Gly	Thr	Asp	Glu	Ile	Ser	Cys	Arg	Ser
			305			310			315			320			
Leu	Phe	Leu	Gly	Ala	Gly	Ser	Leu	Gly	Thr	Thr	Glu	Leu	Leu	Leu	Arg
			325			330			335						
Ala	Arg	Glu	Thr	Gly	Thr	Leu	Pro	Ala	Leu	Ser	Pro	Gln	Ile	Gly	Arg
			340			345			350						

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Gly Trp Gly Gly Asn Gly Asn Val Met Leu Gly Arg Ala Asn His Ile
355 360 365

Trp Asn Thr Thr Gly Ala Asn Gln Ser Thr Ile Pro Val Met Gly Ile
370 375 380

Asp Asp Trp Ser Asn Ala Thr Asn Pro Val Xaa Ala Glu Ile Ala Pro
385 390 395 400

Leu Pro Ala Gly Thr Glu Thr Trp Ala Ser Leu Tyr Leu Ala Ile Thr
405 410 415

Lys Asn Pro Glu Arg Gly Thr Phe Thr Tyr Asp Ala Ala Lys Asp Ala
420 425 430

Ala Val Leu Asn Trp Thr Gly Thr Gln Ser Ala Pro Ser Val Thr Ala
435 440 445

Ala Lys Ser Leu Phe Asp Arg Leu Asn Ser Ala Asn Gly Thr Ile Tyr
450 455 460

Arg Tyr Asp Leu Phe Gly Asp Thr Arg Ala Phe Ala Ala Asp Phe Cys
465 470 475 480

Tyr His Pro Leu Gly Gly Cys Val Leu Gly Arg Ala Thr Asp Ala Tyr
485 490 495

Gly Arg Ala Val Gly Tyr Asp Arg Leu Tyr Val Thr Asp Gly Ser Leu
500 505 510

Ile Pro Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu
515 520 525

Ala Glu Arg Thr Met Ala Arg Val Leu Ala Glu Asp Gly Val Gly
530 535 540

<210> SEQ ID NO 14
<211> LENGTH: 551
<212> TYPE: PRT
<213> ORGANISM: Streptomyces violaceusniger
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (164)...(164)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (233)...(233)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (401)...(401)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa164 is Ile, then Xaa401 is not Phe

<400> SEQUENCE: 14

Met Ala Arg Ser Gly Asp Ser Ala His His Ala Ala Met Thr Ala Asp
1 5 10 15

Leu Thr Arg Arg His Ile Leu Gly Leu Ala Ala Leu Gln Ser Ala Ala
20 25 30

Ala Leu Gly Leu Thr Arg Ile Gly Leu Thr Pro Ala Ala Ala Ala Gln
35 40 45

Arg Ala Asp His Phe Pro Ala Val Val Gly Ser Gly Tyr Gly Ala
50 55 60

Ala Val Ala Ala Leu Arg Leu Gly Glu Ala Gly Ile Arg Thr Leu Val
65 70 75 80

Val Glu Met Gly Arg Leu Trp Asp Thr Pro Gly Pro Asp Gly Arg Val
85 90 95

His Cys Ser Met Thr Ala Pro Asp Gln Arg Ser Met Trp Phe Lys Thr

-continued

100	105	110
Arg Thr Glu Ala Pro Leu Ser Thr Phe Leu Trp Leu Asp Val Ile Asn		
115	120	125
Lys Asp Ile Thr Pro Tyr Pro Gly Val Leu Asp Arg Val Arg Phe Pro		
130	135	140
Gly Met Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser Leu Val		
145	150	155
Asn Gly Xaa Ala Val Thr Pro Ser Arg Ser Tyr Phe Gln Gln Met		
165	170	175
Leu Pro Gln Val Ala Ala Asp Pro Met Tyr Asp Thr Tyr Phe Pro Leu		
180	185	190
Ala Asn Arg Met Leu Gly Ala Asn Thr Val Pro Ser Ala Trp Phe Glu		
195	200	205
Ala Thr Glu Trp Tyr Thr Tyr Ala Arg Val Ala Arg Asp Gln Ala Ala		
210	215	220
Arg Ala Gly Leu Lys Thr Val Phe Xaa Pro Asn Val Tyr Asp Phe Asp		
225	230	235
Tyr Met Arg Arg Glu Ala Asp Gly Thr Ala Thr Lys Ser Ala Leu Ala		
245	250	255
Gln Glu Val Ile Tyr Gly Asn Asn Phe Gly Lys Arg Ser Leu Asp Lys		
260	265	270
Thr Tyr Leu Ala Ala Ala Leu Gly Thr Gly Gln Val Thr Leu His Thr		
275	280	285
Leu Ser Arg Ala Arg Ala Leu Arg Arg Ala Pro Asp Gly Ser Tyr Val		
290	295	300
Leu Thr Val Glu Arg Val Asp Thr Thr Gly Thr Val Val Ser Thr Asp		
305	310	315
Glu Ile Thr Cys Gly Ser Leu Phe Leu Gly Ala Gly Ser Leu Gly Thr		
325	330	335
Thr Glu Leu Leu Leu Arg Ala Arg Glu Thr Gly Ala Leu Pro Glu Leu		
340	345	350
Ser Glu Glu Val Gly Arg Gly Trp Gly Gly Asn Gly Asn Val Met Leu		
355	360	365
Gly Arg Ala Asn His Val Trp His Pro Thr Gly Ala Arg Gln Ser Thr		
370	375	380
Ile Pro Val Met Ala Ile Asp Asp Trp Ser Asn Thr Ala Asn Pro Val		
385	390	395
Xaa Ala Glu Ile Ala Pro Leu Pro Ala Gly Leu Glu Thr Trp Val Ser		
405	410	415
Leu Tyr Leu Ala Ile Thr Arg Asn Pro Glu Arg Ala Thr Phe Thr Tyr		
420	425	430
Asp Ala Ala Lys Asp Ala Ala Val Leu Asp Trp Thr Arg Ala Gln Ser		
435	440	445
Ala Pro Ser Val Ala Ala Lys Ala Leu Phe Asp Arg Val Asn Tyr		
450	455	460
Ala Asn Ala Thr Ile Tyr Arg Tyr Asp Leu Phe Gly Asp Thr Arg Ala		
465	470	475
Ile Ala Asp Asp Phe Cys Tyr His Pro Leu Gly Gly Cys Val Leu Gly		
485	490	495
Arg Ala Thr Asp Pro Tyr Gly Arg Val Thr Gly Tyr Asp Gly Leu Tyr		
500	505	510
Val Thr Asp Gly Ser Leu Ile Pro Gly Ser Ile Gly Val Asn Pro Phe		
515	520	525

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Val Thr Ile Thr Ala Leu Ala Glu Arg Thr Met Ala Arg Val Leu Ala
 530 535 540

Glu Asp Arg Val Gly Ala Arg
 545 550

<210> SEQ_ID NO 15
 <211> LENGTH: 533
 <212> TYPE: PRT
 <213> ORGANISM: Stackebrandtia nassauensis
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (148)..(148)
 <223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
 Tyr, Lys or Ser
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (217)..(217)
 <223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (385)..(385)
 <223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa148 is Met, then Xaa385 is not Phe

<400> SEQUENCE: 15

Met Gly Ile Ser Arg Arg Lys Leu Leu Gly Leu Gly Ala Leu Ala Ala
 1 5 10 15

Gly Ala Ser Ala Gly Val Thr Thr Ile Gly Pro Ala Ala Ala Ala Thr
 20 25 30

Ser Gly Asp Phe Val Pro Ala Leu Val Ile Gly Ser Gly Tyr Gly Ala
 35 40 45

Ala Val Ala Ala Leu Arg Leu Gly Glu Ala Gly Val Arg Thr Thr Ile
 50 55 60

Leu Glu Met Gly Arg Leu Trp His Asp Pro Gly His Asp Gly Lys Ile
 65 70 75 80

Phe Cys Ala Thr Thr Asn Pro Asp His Arg Ser Met Trp Phe Arg His
 85 90 95

Arg Thr Glu Ala Pro Leu Asp Thr Phe Leu Trp Leu Asp Val Val Asn
 100 105 110

Arg Pro Ile Lys Pro Tyr Pro Gly Val Leu Asp Arg Val His Phe Asp
 115 120 125

Glu Met Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser Leu Val
 130 135 140

Asn Gly Gly Xaa Ala Val Val Pro Arg Arg Lys Tyr Phe Gln Gln Val
 145 150 155 160

Leu Pro Glu Val Asp Ala Asp Asp Met Tyr Arg Lys Phe Phe Pro Leu
 165 170 175

Ala Thr Glu Cys Leu Gly Val Asn Asp Ile Asp Thr Asp Tyr Phe Thr
 180 185 190

Asp Ser Asp Tyr Tyr Glu Phe Ala Arg Val Ala Gly Arg Gln Ala Glu
 195 200 205

Glu Thr Gly Leu Ala Thr Thr Phe Xaa Pro Asn Val Tyr Asp Phe Asp
 210 215 220

His Met Ala Arg Glu Glu Ala Gly Thr Ala Thr Lys Ser Ala Leu Ala
 225 230 235 240

Ala Glu Val Ile Tyr Gly Asn Asn His Gly Lys Arg Ser Leu Asp His
 245 250 255

Ser Tyr Leu Ala Ser Ala Leu Gly Thr Gly Asn Val Thr Ile Glu Thr

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260	265	270
Leu His Gln Val Arg Asp Ile Arg Gln Asn Arg Asp Gly Ser Tyr Val		
275	280	285
Val Thr Val Asp His Ile Asp Glu Thr Gly Glu Val Val Glu Ser Lys		
290	295	300
Gln Ile Gly Cys Arg His Leu Phe Leu Gly Ala Gly Ser Leu Gly Thr		
305	310	315
Thr Glu Leu Leu Leu Arg Ala Arg Asp Thr Gly Ala Leu Pro Asp Leu		
325	330	335
Asp Ala Asp Val Gly Gln Gly Trp Gly Pro Asn Gly Asn Ile Met Ala		
340	345	350
Gly Arg Ala Asn Asn Ala Ser Gln Pro Thr Gly Ala Arg Gln Ser Ala		
355	360	365
Ile Pro Val Leu Ala Ile Asp Asp Trp Asp Asn Glu Ala Ala Arg Val		
370	375	380
Xaa Ala Glu Ile Ala Pro Val Pro Ala Gly Phe Glu Thr Trp Ile Ser		
385	390	395
Met Tyr Leu Ala Ile Thr Glu Asn Pro Glu Arg Ala Ser Phe Arg Tyr		
405	410	415
Asp Pro Ala Thr Asp Arg Ala Val Leu Asp Trp Arg Arg Asp Gln Asn		
420	425	430
Thr Pro Ser Val Ala Ser Ala Lys Ser Leu Leu Asp Arg Ile Asn Glu		
435	440	445
Thr Gln Lys Thr Thr Tyr Arg His Asp Leu Phe Gly Asp Asp Arg Ala		
450	455	460
Phe Ala Asp Asp Phe Cys Tyr His Pro Leu Gly Gly Cys Val Leu Gly		
465	470	475
Asn Ala Thr Asp Asn Tyr Gly Arg Leu Lys Gly Tyr Arg Asn Leu Tyr		
485	490	495
Ala Thr Asp Gly Ala Leu Ile Pro Gly Ser Leu Gly Val Asn Pro Phe		
500	505	510
Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Met Ala Lys Ile Ile Ala		
515	520	525
Thr Asp Ile Thr Thr		
530		

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<210> SEQ ID NO 16
<211> LENGTH: 545
<212> TYPE: PRT
<213> ORGANISM: Streptomyces clavuligerus
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (154)..(154)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (223)..(223)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (397)..(397)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa154 is Met, then Xaa397 is not Phe

<400> SEQUENCE: 16

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Met Thr Pro His Leu Thr Arg Arg Gln Leu Met Gly Ala Ala Ala Leu		
1	5	10
		15

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Gln Thr Ala Ala Val Leu Gly Phe Thr Arg Val Gly Leu Ser Ser Ala
20 25 30

His Ala Val Glu Pro Pro Ala Ala Pro His Ala Pro Ala Val Val Ile
35 40 45

Gly Ser Gly Tyr Gly Ala Ala Val Ala Ala Leu Arg Leu Gly Leu Ala
50 55 60

Gly Val Pro Thr Leu Val Leu Glu Met Gly Arg Leu Trp Asp Thr Ala
65 70 75 80

Gly Pro Asp Gly Lys Val Phe Cys Pro Thr Ile Thr Pro Asp Arg Arg
85 90 95

Ser Met Trp Phe Arg Thr Arg Thr Glu Ala Pro Leu Ser Thr Phe Leu
100 105 110

Trp Leu Asp Val Val Asn Arg Arg Ile Asp Pro Tyr Pro Gly Val Leu
115 120 125

Asp Arg Val Asn Tyr Gly Asp Met Ser Val Tyr Val Gly Arg Gly Val
130 135 140

Gly Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Pro Arg
145 150 155 160

Pro Tyr Phe Ser Glu Val Leu Pro Gly Val Asp Ala Glu Ala Met Tyr
165 170 175

Gly Thr Tyr Phe Pro Arg Ala Arg Met Leu Gly Val Asn Glu Val
180 185 190

Asp Arg Ser Trp Phe Glu Ser Thr Pro Trp Tyr Arg Phe Ser Arg Val
195 200 205

Ser Arg Thr His Ala Ala Arg Ala Gly Leu Gly Thr Val Phe Xaa Pro
210 215 220

Asn Val Tyr Asp Phe Asp Tyr Met Arg Arg Glu Ala Ala Gly Glu Val
225 230 235 240

Pro Arg Ser Ala Leu Ala Gly Glu Val Ile Tyr Gly Asn Asn His Gly
245 250 255

Lys Arg Ser Leu Asp Arg Thr Tyr Leu Ala Ala Leu Ala Thr Gly
260 265 270

Arg Val Thr Val Glu Thr Met Ser Arg Val Arg Ala Leu Arg Pro Ala
275 280 285

Asn Thr Gly Gly Thr Gly Ala Gly Gly Tyr Val Leu Thr Val Glu
290 295 300

Arg Leu Asp Leu Ser Gly Arg Val Thr Ala Val Asp Glu Ile Thr Thr
305 310 315 320

Gly Arg Leu Phe Leu Gly Ala Gly Ser Leu Gly Thr Thr Glu Leu Leu
325 330 335

Leu Arg Ala Arg Glu Thr Gly Ala Leu Pro Asp Leu Asp Pro Glu Val
340 345 350

Gly Arg Gly Trp Gly His Asn Gly Asn Val Met Thr Ala Arg Ala Asn
355 360 365

His Leu Trp Asp Thr Val Gly Ala Gln Gln Ser Thr Met Pro Val Leu
370 375 380

Gly Ile Asp Asp Trp Asn Asn Pro Thr His Pro Val Xaa Ala Glu Ile
385 390 395 400

Ala Pro Leu Pro Met Gly Leu Glu His Trp Ile Ser Leu Tyr Leu Ala
405 410 415

Ile Thr Lys Asn Pro Glu Arg Gly His Phe Thr Tyr Asp Ala Ala Thr
420 425 430

Asp Ser Ala Arg Leu Arg Trp Thr Arg Asp Gln Asn Glu Pro Ser Val

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435 440 445

Ala Ala Ala Arg Ser Leu Phe Asp Arg Ile Asn Arg Ala Asn Gly Thr
450 455 460

Ile His Arg Tyr Asp Leu Phe Gly Gly Asn Arg Lys Phe Ala Asp Asp
465 470 475 480

Phe Thr Tyr His Pro Leu Gly Gly Cys Val Leu Gly Arg Ala Thr Asp
485 490 495

Gly Tyr Gly Arg Ala Lys Gly His Pro Gly Leu Tyr Val Val Asp Gly
500 505 510

Ser Leu Val Pro Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile Thr
515 520 525

Ala Leu Ala Glu Arg Asn Met Glu Arg Ile Val Gln Glu Asp Ile Leu
530 535 540

Gly
545

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<210> SEQ_ID NO 17
<211> LENGTH: 559
<212> TYPE: PRT
<213> ORGANISM: Streptomyces clavuligerus
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (168)..(168)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (237)..(237)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (411)..(411)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa168 is Met, then Xaa411 is not Phe

<400> SEQUENCE: 17
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Met Ala Leu Gly Ile Arg Pro Val Leu Val Asp Asp Gln His Met Thr
1 5 10 15

Pro His Leu Thr Arg Arg Gln Leu Met Gly Ala Ala Ala Leu Gln Thr
20 25 30

Ala Ala Val Leu Gly Phe Thr Arg Val Gly Leu Ser Ser Ala His Ala
35 40 45

Val Glu Pro Pro Ala Ala Pro His Ala Pro Ala Val Val Ile Gly Ser
50 55 60

Gly Tyr Gly Ala Ala Val Ala Ala Leu Arg Leu Gly Leu Ala Gly Val
65 70 75 80

Pro Thr Leu Val Leu Glu Met Gly Arg Leu Trp Asp Thr Ala Gly Pro
85 90 95

Asp Gly Lys Val Phe Cys Pro Thr Ile Thr Pro Asp Arg Arg Ser Met
100 105 110

Trp Phe Arg Thr Arg Thr Glu Ala Pro Leu Ser Thr Phe Leu Trp Leu
115 120 125

Asp Val Val Asn Arg Arg Ile Asp Pro Tyr Pro Gly Val Leu Asp Arg
130 135 140

Val Asn Tyr Gly Asp Met Ser Val Tyr Val Gly Arg Gly Val Gly Gly
145 150 155 160

Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Pro Arg Pro Tyr
165 170 175

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Phe Ser Glu Val Leu Pro Gly Val Asp Ala Glu Ala Met Tyr Gly Thr
180 185 190

Tyr Phe Pro Arg Ala Arg Arg Met Leu Gly Val Asn Glu Val Asp Arg
195 200 205

Ser Trp Phe Glu Ser Thr Pro Trp Tyr Arg Phe Ser Arg Val Ser Arg
210 215 220

Thr His Ala Ala Arg Ala Gly Leu Gly Thr Val Phe Xaa Pro Asn Val
225 230 235 240

Tyr Asp Phe Asp Tyr Met Arg Arg Glu Ala Ala Gly Glu Val Pro Arg
245 250 255

Ser Ala Leu Ala Gly Glu Val Ile Tyr Gly Asn Asn His Gly Lys Arg
260 265 270

Ser Leu Asp Arg Thr Tyr Leu Ala Ala Leu Ala Thr Gly Arg Val
275 280 285

Thr Val Glu Thr Met Ser Arg Val Arg Ala Leu Arg Pro Ala Asn Thr
290 295 300

Gly Gly Thr Gly Ala Gly Gly Tyr Val Leu Thr Val Glu Arg Leu
305 310 315 320

Asp Leu Ser Gly Arg Val Thr Ala Val Asp Glu Ile Thr Thr Gly Arg
325 330 335

Leu Phe Leu Gly Ala Gly Ser Leu Gly Thr Thr Glu Leu Leu Arg
340 345 350

Ala Arg Glu Thr Gly Ala Leu Pro Asp Leu Asp Pro Glu Val Gly Arg
355 360 365

Gly Trp Gly His Asn Gly Asn Val Met Thr Ala Arg Ala Asn His Leu
370 375 380

Trp Asp Thr Val Gly Ala Gln Gln Ser Thr Met Pro Val Leu Gly Ile
385 390 395 400

Asp Asp Trp Asn Asn Pro Thr His Pro Val Xaa Ala Glu Ile Ala Pro
405 410 415

Leu Pro Met Gly Leu Glu His Trp Ile Ser Leu Tyr Leu Ala Ile Thr
420 425 430

Lys Asn Pro Glu Arg Gly His Phe Thr Tyr Asp Ala Ala Thr Asp Ser
435 440 445

Ala Arg Leu Arg Trp Thr Arg Asp Gln Asn Glu Pro Ser Val Ala Ala
450 455 460

Ala Arg Ser Leu Phe Asp Arg Ile Asn Arg Ala Asn Gly Thr Ile His
465 470 475 480

Arg Tyr Asp Leu Phe Gly Gly Asn Arg Lys Phe Ala Asp Asp Phe Thr
485 490 495

Tyr His Pro Leu Gly Gly Cys Val Leu Gly Arg Ala Thr Asp Gly Tyr
500 505 510

Gly Arg Ala Lys Gly His Pro Gly Leu Tyr Val Val Asp Gly Ser Leu
515 520 525

Val Pro Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu
530 535 540

Ala Glu Arg Asn Met Glu Arg Ile Val Gln Glu Asp Ile Leu Gly
545 550 555

<210> SEQ ID NO 18
<211> LENGTH: 534
<212> TYPE: PRT
<213> ORGANISM: Saccharopolyspora erythraea
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE

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<222> LOCATION: (151)..(151)
 <223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln, Tyr, Lys or Ser
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (220)..(220)
 <223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser, Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (388)..(388)
 <223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His or Asp, provided that when Xaa151 is Met, then Xaa388 is not Phe

<400> SEQUENCE: 18

Met	Thr	Ser	Ser	Val	Thr	Arg	Arg	Arg	Phe	Leu	Gly	Met	Ala	Ala	Met
1									5		10				15

Gln	Ser	Ala	Ala	Val	Leu	Gly	Leu	Gly	Ala	Val	Ser	Leu	Gly	Arg	Ala
									20		25				30

Asp	Ala	Ala	Glu	Arg	Pro	Phe	Val	Pro	Ala	Val	Val	Val	Gly	Ser	Gly
									35		40				45

Tyr	Gly	Ser	Ala	Ala	Thr	Ala	Leu	Arg	Leu	Gly	Glu	Ala	Gly	Val	Ser
									50		55				60

Thr	Leu	Val	Leu	Glu	Met	Gly	Arg	Leu	Trp	Asp	Arg	Ala	Gly	Glu	Asp
65									70		75				80

Gly	Ala	Ile	Phe	Cys	Ser	Met	Leu	Gln	Pro	Asp	His	Arg	Ala	Met	Trp
									85		90				95

Phe	Lys	Ala	Arg	Thr	Glu	Ala	Pro	Leu	Ser	Ser	Leu	Leu	Trp	Met	Asp
									100		105				110

Leu	Val	Asn	Arg	Asp	Ile	Lys	Pro	Phe	Ala	Gly	Val	Leu	Asp	Arg	Val
									115		120				125

His	His	Gly	Asp	Met	Ser	Val	Tyr	Val	Gly	Arg	Gly	Val	Gly	Gly	Gly
									130		135				140

Ser	Leu	Val	Asn	Gly	Gly	Xaa	Ala	Val	Thr	Pro	Arg	Arg	Gly	Tyr	Phe
145									150		155				160

Glu	Glu	Val	Leu	Pro	Arg	Val	Asp	Ala	Gly	Glu	Met	Tyr	Gly	Arg	Phe
								165		170				175	

Phe	Pro	Leu	Ala	Asn	Arg	Met	Leu	Gly	Val	Asn	Thr	Val	Asp	Arg	Thr
									180		185				190

Trp	Phe	Glu	Glu	Cys	Glu	Ser	Tyr	Arg	Tyr	Ala	Arg	Val	Ser	Arg	Gly
									195		200				205

His	Ala	Gln	Arg	Ala	Gly	Leu	Arg	Thr	Thr	Phe	Xaa	Pro	Asn	Val	Tyr
									210		215				220

Asp	Phe	Gly	Tyr	Met	Arg	Arg	Glu	Glu	Arg	Gly	Glu	Val	Pro	Lys	Ser
225									225		230				240

Ala	Leu	Ser	Ser	Glu	Val	Ile	Tyr	Gly	Asn	Asn	His	Gly	Lys	Arg	Ser
									245		250				255

Leu	Asp	Arg	Ser	Tyr	Leu	Pro	Ala	Ala	Val	Gly	Thr	Gly	Asn	Val	Thr
									260		265				270

Ile	Gln	Ser	Leu	His	Arg	Val	Arg	Ser	Phe	Arg	Gln	Glu	Pro	Asp	Gly
									275		280				285

Thr	Tyr	Val	Leu	Thr	Val	Glu	Arg	Ile	Asp	Glu	Leu	Gly	Asn	Met	Leu
									290		295				300

Gly	Thr	Thr	Glu	Ile	Gly	Cys	Arg	Trp	Leu	Phe	Leu	Gly	Ala	Gly	Ser
									305		310				320

Met	Gly	Thr	Thr	Glu	Leu	Leu	Arg	Ala	Arg	Glu	Thr	Gly	Val	Leu	
									325		330				335

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Pro Arg Leu Asp Asp Ser Val Gly His Gly Trp Gly Thr Asn Gly Asn
340 345 350

Val Met Leu Gly Arg Ala Leu His Ser Trp Asp Arg Thr Gly Ser Val
355 360 365

Gln Ser Gly Met Pro Ala Leu Gly Ile Asp Asn Trp Asp Asp Pro Val
370 375 380

His Pro Val Xaa Ala Glu Ile Ala Pro Leu Pro Ala Gly Leu Glu Leu
385 390 395 400

Leu Thr Ser Leu Ser Ala Ile Thr Arg Asn Pro Glu Arg Gly Ser
405 410 415

Phe Ser Tyr Asp Pro Ala Ala Asp Ala Ala Arg Leu His Trp Ser Ala
420 425 430

Ser Gln Gly Lys Pro Ser Val Glu Ala Ala Lys Ala Leu Phe Asp Pro
435 440 445

Ile Asn Arg Ala Asn Gly Thr Val Tyr Arg His Asp Leu Phe Gly Asp
450 455 460

Ser Arg Ala Phe Glu Asp Arg Phe Thr Tyr His Pro Leu Gly Gly Cys
465 470 475 480

Val Leu Gly Glu Ala Thr Asp Asp Phe Gly Arg Val Arg Gly Tyr Arg
485 490 495

Asn Leu Tyr Val Thr Asp Gly Ser Leu Ile Pro Gly Ser Thr Gly Val
500 505 510

Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Asp Arg
515 520 525

Val Leu Ser Glu Asp Phe
530

<210> SEQ ID NO 19
<211> LENGTH: 544
<212> TYPE: PRT
<213> ORGANISM: Streptomyces avermitilis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (159)..(159)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (228)..(228)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (396)..(396)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa159 is Met, then Xaa396 is not Phe
<400> SEQUENCE: 19

Met Thr Glu Lys Leu Thr His Arg His Leu Thr Arg Arg Gln Ile Leu
1 5 10 15

Gly Met Ala Ala Leu Gln Thr Ala Ala Thr Leu Gly Phe Thr Arg Ile
20 25 30

Gly Leu Gln Ser Ala Arg Ala Ala Glu Pro Asp Ala Val Glu Thr Ala
35 40 45

Pro Ala Ile Val Val Gly Ser Gly Tyr Gly Ala Ala Val Ala Ala Leu
50 55 60

Arg Leu Gly Gln Ala Gly Leu Arg Thr Leu Val Ile Glu Met Gly Gly
65 70 75 80

Leu Trp Asn Thr Pro Gly Ser Asp Gly Lys Val Phe Cys Ser Thr Ser
85 90 95

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Ala Pro Asp Arg Arg Ser Met Trp Phe Arg Thr Arg Thr Glu Ala Pro
 100 105 110
 Leu Ala Glu Phe Leu Trp Leu Asp Val Val Asn Lys Asp Ile Ser Pro
 115 120 125
 Tyr Pro Gly Val Leu Asp Arg Val His Phe Ala Asn Met Ser Val Tyr
 130 135 140
 Val Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala
 145 150 155 160
 Val Thr Pro Leu Gln Ser Tyr Phe Ala Glu Gln Phe Pro Thr Val Asp
 165 170 175
 Ala Ala Glu Met Tyr Ser Thr Tyr Phe Pro Arg Ala Arg Thr Met Leu
 180 185 190
 Gly Val Asn Thr Val Asp Pro Ala Trp Phe Glu Ser Thr Glu Trp Tyr
 195 200 205
 Arg Phe Thr Arg Thr Ser Arg Lys Ala Ala Thr Asn Thr Gly Leu Lys
 210 215 220
 Thr Thr Phe Xaa Pro Asn Val Tyr Asp Phe Gly Tyr Met Gln Arg Glu
 225 230 235 240
 Ala Ala Gly Thr Ala Thr Lys Ser Ala Leu Ala Gly Glu Val Ile Tyr
 245 250 255
 Gly Asn Asn Tyr Gly Lys Arg Ser Leu Asp Lys Thr Tyr Leu Ala Ser
 260 265 270
 Ala Leu Gly Thr Gly Asn Val Thr Ile His Thr Leu Glu Arg Val Arg
 275 280 285
 Glu Ile Arg Arg Ala Ser Asp Gly Thr Tyr Leu Leu Thr Ala Asp Arg
 290 295 300
 Ile Asp Thr Thr Gly Ala Val Val Glu Thr Lys Gln Tyr Ser Cys Thr
 305 310 315 320
 Tyr Leu Phe Leu Gly Gly Ser Leu Gly Thr Ser Glu Leu Leu Val
 325 330 335
 Arg Ala Arg Glu Thr Gly Ala Leu Pro Ala Leu Asp Ala Ser Val Gly
 340 345 350
 Thr Gly Trp Gly Thr Asn Gly Asn Val Met Thr Gly Arg Ala Asn His
 355 360 365
 Ile Trp Asp Thr Val Gly Ala Asn Gln Ser Thr Met Pro Val Met Gly
 370 375 380
 Ile Asp Asp Trp Ala Asn Thr Ser Asn Pro Val Xaa Ala Glu Ile Ala
 385 390 395 400
 Pro Leu Pro Met Gly Leu Glu His Trp Ile Ser Leu Tyr Leu Ala Ile
 405 410 415
 Thr Lys Asn Pro Glu Arg Ala Ser Phe Thr Tyr Asp Ala Ala Ser Asp
 420 425 430
 Ser Ala Lys Leu Gly Trp Ser Ala Ala Gln Ser Ala Val Ser Val Ser
 435 440 445
 Met Ala Lys Lys Leu Phe Asp Arg Ile Asn Ser Ala Asn Ala Thr Ile
 450 455 460
 Tyr Arg Tyr Asp Leu Phe Gly Asn Asn Lys Thr Phe Ala Asp Asp Phe
 465 470 475 480
 Thr Tyr His Pro Leu Gly Gly Cys Val Leu Gly Lys Ser Thr Asp Asn
 485 490 495
 Tyr Gly Arg Val Lys Gly Tyr Ser Lys Leu Tyr Val Thr Asp Gly Ser
 500 505 510

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Leu Val Pro Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile Thr Ala
515 520 525

Leu Ala Glu Arg Thr Met Ala Arg Val Leu Ala Glu Asp Thr Ala Pro
530 535 540

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<210> SEQ ID NO 20
<211> LENGTH: 522
<212> TYPE: PRT
<213> ORGANISM: Saccharopolyspora erythraea
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (139) ..(139)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (208) ..(208)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (376) ..(376)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa139 is Met, then Xaa376 is not Phe

<400> SEQUENCE: 20

```

Met Ala Ala Met Gln Ser Ala Ala Val Leu Gly Leu Gly Ala Val Ser
1 5 10 15

Leu Gly Arg Ala Asp Ala Ala Glu Arg Pro Phe Val Pro Ala Val Val
20 25 30

Val Gly Ser Gly Tyr Gly Ser Ala Ala Thr Ala Leu Arg Leu Gly Glu
35 40 45

Ala Gly Val Ser Thr Leu Val Leu Glu Met Gly Arg Leu Trp Asp Arg
50 55 60

Ala Gly Glu Asp Gly Ala Ile Phe Cys Ser Met Leu Gln Pro Asp His
65 70 75 80

Arg Ala Met Trp Phe Lys Ala Arg Thr Glu Ala Pro Leu Ser Ser Leu
85 90 95

Leu Trp Met Asp Leu Val Asn Arg Asp Ile Lys Pro Phe Ala Gly Val
100 105 110

Leu Asp Arg Val His His Gly Asp Met Ser Val Tyr Val Gly Arg Gly
115 120 125

Val Gly Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Arg
130 135 140

Arg Gly Tyr Phe Glu Glu Val Leu Pro Arg Val Asp Ala Gly Glu Met
145 150 155 160

Tyr Gly Arg Phe Pro Leu Ala Asn Arg Met Leu Gly Val Asn Thr
165 170 175

Val Asp Arg Thr Trp Phe Glu Glu Cys Glu Ser Tyr Arg Tyr Ala Arg
180 185 190

Val Ser Arg Gly His Ala Gln Arg Ala Gly Leu Arg Thr Thr Phe Xaa
195 200 205

Pro Asn Val Tyr Asp Phe Gly Tyr Met Arg Arg Glu Glu Arg Gly Glu
210 215 220

Val Pro Lys Ser Ala Leu Ser Ser Glu Val Ile Tyr Gly Asn Asn His
225 230 235 240

Gly Lys Arg Ser Leu Asp Arg Ser Tyr Leu Pro Ala Ala Val Gly Thr
245 250 255

Gly Asn Val Thr Ile Gln Ser Leu His Arg Val Arg Ser Phe Arg Gln
260 265 270

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Glu Pro Asp Gly Thr Tyr Val Leu Thr Val Glu Arg Ile Asp Glu Leu
275 280 285

Gly Asn Met Leu Gly Thr Thr Glu Ile Gly Cys Arg Trp Leu Phe Leu
290 295 300

Gly Ala Gly Ser Met Gly Thr Thr Glu Leu Leu Leu Arg Ala Arg Glu
305 310 315 320

Thr Gly Val Leu Pro Arg Leu Asp Asp Ser Val Gly His Gly Trp Gly
325 330 335

Thr Asn Gly Asn Val Met Leu Gly Arg Ala Leu His Ser Trp Asp Arg
340 345 350

Thr Gly Ser Val Gln Ser Gly Met Pro Ala Leu Gly Ile Asp Asn Trp
355 360 365

Asp Asp Pro Val His Pro Val Xaa Ala Glu Ile Ala Pro Leu Pro Ala
370 375 380

Gly Leu Glu Leu Leu Thr Ser Leu Ser Leu Ala Ile Thr Arg Asn Pro
385 390 395 400

Glu Arg Gly Ser Phe Ser Tyr Asp Pro Ala Ala Asp Ala Ala Arg Leu
405 410 415

His Trp Ser Ala Ser Gln Gly Lys Pro Ser Val Glu Ala Ala Lys Ala
420 425 430

Leu Phe Asp Pro Ile Asn Arg Ala Asn Gly Thr Val Tyr Arg His Asp
435 440 445

Leu Phe Gly Asp Ser Arg Ala Phe Glu Asp Arg Phe Thr Tyr His Pro
450 455 460

Leu Gly Gly Cys Val Leu Gly Glu Ala Thr Asp Asp Phe Gly Arg Val
465 470 475 480

Arg Gly Tyr Arg Asn Leu Tyr Val Thr Asp Gly Ser Leu Ile Pro Gly
485 490 495

Ser Thr Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg
500 505 510

Asn Ile Asp Arg Val Leu Ser Glu Asp Phe
515 520

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<210> SEQ_ID NO 21
<211> LENGTH: 547
<212> TYPE: PRT
<213> ORGANISM: Streptomyces hygroscopicus
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (161)..(161)
<223> OTHER_INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (230)..(230)
<223> OTHER_INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (398)..(398)
<223> OTHER_INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa161 is Ile, then Xaa398 is not Phe

<400> SEQUENCE: 21

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Met Ser His Ser Ala His Asp Ala Ala Met Glu Gly Lys Leu Thr Arg
1 5 10 15

Arg His Phe Leu Gly Leu Ala Ala Leu Gln Thr Ala Ala Leu Gly
20 25 30

Leu Thr Arg Ile Gly Leu Thr Pro Ala Ala Ala Gln Ser Ala Asp

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35 40 45

His Thr Pro Ala Leu Val Ile Gly Ser Gly Tyr Gly Ala Ala Val Ala
 50 55 60

Ala Leu Arg Leu Gly Glu Ala Gly Ile Arg Thr Leu Val Ile Glu Met
 65 70 75 80

Gly Arg Leu Trp Glu Ala Pro Asp Ser Gly Gly Thr Val Phe Cys Ser
 85 90 95

Met Thr Ala Pro Asp Gln Arg Ser Met Trp Phe Lys Arg Arg Thr Glu
 100 105 110

Ala Pro Leu Ser Thr Phe Leu Trp Leu Asp Val Ile Asn Lys Asp Ile
 115 120 125

Thr Pro Tyr Pro Gly Val Leu Asp Arg Val Arg His Pro Asn Met Ser
 130 135 140

Val Tyr Val Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly Gly
 145 150 155 160

Xaa Ala Val Thr Pro Pro Arg Ala Tyr Phe Gln Glu Val Leu Pro Gly
 165 170 175

Val Asp Ala Asp Ala Met Tyr Gly Thr Tyr Phe Pro Arg Ala Asn Arg
 180 185 190

Met Leu Gly Thr Ala Thr Ile Pro Ser Asp Trp Phe Glu Gly Thr Glu
 195 200 205

Trp Tyr Gln Tyr Ala Arg Val Ala Arg Ala Gln Ala Ser Ala Ala Gly
 210 215 220

Leu Lys Thr Val Phe Xaa Pro Ser Val Tyr Asp Phe Asp Tyr Met Arg
 225 230 235 240

Arg Glu Ala Ala Gly Thr Ala Thr Lys Ser Ala Leu Ala Gln Glu Val
 245 250 255

Ile Tyr Gly Asn Asn His Gly Lys Arg Ser Leu Asp Lys Thr Tyr Leu
 260 265 270

Ala Ala Ala Leu Gly Thr Gly Asn Val Thr Ile His Thr Leu Ser Arg
 275 280 285

Ala Arg Ala Ile Arg Arg Ala Ala Asp Gly Ser Tyr Thr Val Thr Val
 290 295 300

Asp Arg Ile Asp Thr Thr Gly Ala Val Thr Ala Thr Asp Glu Ile Ser
 305 310 315 320

Cys Arg Ala Leu Phe Leu Gly Ala Gly Ser Leu Gly Thr Thr Glu Leu
 325 330 335

Leu Leu Arg Ala Arg Glu Thr Gly Thr Leu Pro Gly Leu Asn Ala Glu
 340 345 350

Val Gly Arg Gly Trp Gly Gly Asn Gly Asn Val Met Leu Gly Arg Ala
 355 360 365

Asn His Val Trp Asn Pro Thr Gly Ala His Gln Ser Thr Ile Pro Val
 370 375 380

Thr Ala Ile Asp Asp Trp Ser Asn Ala Ala Asn Pro Val Xaa Ala Glu
 385 390 395 400

Ile Ala Pro Leu Pro Ala Gly Thr Glu Thr Trp Ala Ser Leu Tyr Leu
 405 410 415

Ala Ile Thr Lys Asn Pro Glu Arg Gly Thr Phe Thr Tyr Asp Ala Ala
 420 425 430

Lys Asp Ala Ala Val Leu Asn Trp Thr Ala Gly Gln Ser Ala Pro Ala
 435 440 445

Ile Ala Ala Ala Lys Ala Leu Phe Asp Arg Val Asn Ala Ala Asn Val
 450 455 460

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Thr Ile Tyr Arg Tyr Asp Leu Phe Gly Asp Thr Arg Ala Phe Ala Ala
 465 470 475 480

Asp Phe Cys Tyr His Pro Leu Gly Gly Cys Val Leu Gly Arg Ala Thr
 485 490 495

Asp Ala Tyr Gly Arg Val Ala Gly Tyr Pro Arg Leu Tyr Val Thr Asp
 500 505 510

Gly Ser Leu Ile Pro Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile
 515 520 525

Thr Ala Leu Ala Glu Arg Thr Met Ala Arg Val Leu Ala Glu Asp Asp
 530 535 540

Val Gly Arg
 545

<210> SEQ ID NO 22
<211> LENGTH: 545
<212> TYPE: PRT
<213> ORGANISM: Streptomyces viridochromogenes
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (159)..(159)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
 Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (228)..(228)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (396)..(396)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa159 is Met, then Xaa396 is not Phe

<400> SEQUENCE: 22

Met Thr Val Lys Leu Met Gln Arg Gln Leu Thr Arg Arg Gln Ile Leu
 1 5 10 15

Gly Met Val Ala Leu Gln Gly Ala Ala Ala Ala Gly Leu Thr Arg Ile
 20 25 30

Gly Leu Gln Val Ala Ser Ala Ala Glu Pro Ala Ala Val Asp Asn Ala
 35 40 45

Pro Ala Ile Val Val Gly Ser Gly Tyr Gly Ala Val Ala Ala Leu
 50 55 60

Arg Leu Gly Gln Ala Gly Ile Arg Thr Leu Val Leu Glu Met Gly Arg
 65 70 75 80

Leu Trp Asn Thr Pro Gly Pro Asp Gly Lys Val Phe Cys Ser Thr Arg
 85 90 95

Thr Pro Asp Gln Arg Ser Met Trp Phe Arg Thr Arg Thr Glu Ala Pro
 100 105 110

Leu Ala Thr Phe Leu Trp Leu Asp Leu Val Asn Gln Asp Ile Ser Ser
 115 120 125

Tyr Pro Gly Val Leu Asp Arg Val His Tyr Asp His Met Ser Val Tyr
 130 135 140

Val Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala
 145 150 155 160

Val Thr Pro Leu Arg Ser Tyr Phe Ala Glu Gln Phe Pro Thr Val Asp
 165 170 175

Thr Ala Glu Met Tyr Asp Thr Tyr Phe Pro Arg Ala Arg Ser Met Leu
 180 185 190

Gly Val Asn Thr Val Asp Pro Ala Trp Phe Glu Ser Thr Glu Trp Tyr

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195 200 205

Arg Phe Thr Arg Ile Ser Arg Lys His Ala Asp Asn Ala Gly Leu Lys
 210 215 220

Thr Thr Phe Xaa Pro Asn Val Tyr Asp Phe Gly His Met Glu Arg Glu
 225 230 235 240

Ala Ala Gly Thr Ala Thr Lys Ser Ala Leu Ala Gly Glu Val Ile Tyr
 245 250 255

Gly Asn Asn Gln Gly Lys Arg Ser Leu Asp Lys Thr Tyr Leu Ala Ser
 260 265 270

Ala Leu Gly Thr Gly Asn Val Thr Leu His Thr Met Glu Arg Val Thr
 275 280 285

Ser Ile Ser Arg Ala Ala Asp Gly Thr Tyr Leu Leu Thr Ala Asp Arg
 290 295 300

Ile Asp Asp Thr Gly Thr Val Val Glu Thr Lys Glu Tyr Ala Cys Thr
 305 310 315 320

Tyr Leu Phe Leu Gly Gly Ser Ile Gly Thr Thr Glu Leu Leu Val
 325 330 335

Arg Ala Arg Glu Ser Gly Thr Leu Pro Arg Leu Asp Ala Ser Val Gly
 340 345 350

Thr Gly Trp Gly Thr Asn Gly Asn Val Met Leu Gly Arg Ala Asn His
 355 360 365

Val Trp Asp Thr Val Gly Ala Asn Gln Ser Thr Met Pro Val Met Gly
 370 375 380

Ile Asp Asp Trp Ala Asn Thr Ala Asn Pro Val Xaa Ala Glu Ile Ala
 385 390 395 400

Pro Leu Pro Met Gly Leu Glu His Trp Val Ser Leu Tyr Leu Ala Ile
 405 410 415

Thr Lys Asn Pro Glu Arg Ala Ser Phe Thr Tyr Asp Pro Ala Ser Gly
 420 425 430

Ala Val Arg Leu Gly Trp Ser Ala Ala Gln Ser Ala Val Ser Val Gly
 435 440 445

Met Ala Lys Lys Leu Phe Asp Arg Ile Asn Lys Ala Asn Ala Thr Ile
 450 455 460

Tyr Arg Tyr Asp Leu Phe Gly Ser Ser Asn Lys Val Phe Ala Asp Asp
 465 470 475 480

Phe Thr Tyr His Pro Leu Gly Gly Cys Val Leu Gly Arg Ser Thr Asp
 485 490 495

Ala Tyr Gly Arg Val Lys Gly Tyr Ser Arg Leu Tyr Val Thr Asp Gly
 500 505 510

Ser Leu Val Pro Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile Thr
 515 520 525

Ala Leu Ala Glu Arg Thr Met Ala Arg Val Leu Ala Glu Asp Thr Ala
 530 535 540

Pro
 545

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<210> SEQ_ID NO 23
<211> LENGTH: 531
<212> TYPE: PRT
<213> ORGANISM: Microscilla marina
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (146)...(146)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
  Tyr, Lys, or Ser
<220> FEATURE:

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<221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (215)...(215)
 <223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (383)...(383)
 <223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa146 is Met, then Xaa383 is not Phe

<400> SEQUENCE: 23

Met	Gly	Ser	Ala	Ser	Val	Met	Gly	Leu	Thr	Thr	Ile	Ser	Leu	Ala	Asn
1															
								10							15

Cys	Phe	Asn	Pro	Thr	Leu	Pro	Gln	Lys	Glu	Lys	Asn	Arg	Asn	Glu	Thr
								20	25	30					

Thr	His	Phe	Thr	Ser	Ile	Val	Ile	Gly	Thr	Gly	Tyr	Gly	Gly	Ala	Val
								35	40	45					

Ser	Ala	Leu	Arg	Leu	Gly	Glu	Ala	Gly	Val	Asp	Thr	Leu	Met	Leu	Glu
								50	55	60					

Met	Gly	Gln	Leu	Trp	Asp	Lys	Pro	Gly	Pro	Asp	Gly	Lys	Val	Phe	Cys
								65	70	75	80				

Lys	Met	Thr	Lys	Pro	Asp	Gly	Arg	Ala	Met	Trp	Phe	Lys	Asn	Arg	Thr
								85	90	95					

Glu	Ala	Pro	Leu	Ser	Ser	Phe	Leu	Trp	Ile	Asp	Ala	Ile	Asn	Arg	Pro
								100	105	110					

Ile	Asp	Tyr	Tyr	Ala	Gly	Val	Leu	Asp	Arg	Ile	Asn	Tyr	Pro	Asn	Met
								115	120	125					

Ser	Val	Tyr	Val	Gly	Arg	Gly	Val	Gly	Gly	Ser	Leu	Val	Asn	Gly
								130	135	140				

Gly	Xaa	Ala	Val	Thr	Pro	Pro	Met	Asn	Tyr	Phe	Gln	Glu	Ile	Leu	Pro
								145	150	155	160				

Glu	Val	Asn	Thr	His	Glu	Met	Tyr	Asn	Lys	Tyr	Phe	Pro	Arg	Ala	Asn
								165	170	175					

Gln	Lys	Leu	Gln	Val	Asn	Thr	Ile	Pro	Asn	Thr	Leu	Glu	Asn	Ser
								180	185	190				

Pro	Tyr	Tyr	Arg	Phe	Thr	Arg	Val	Gly	Arg	Gln	Gln	Ala	Glu	Lys	Ala
								195	200	205					

Gly	Phe	Lys	Thr	Val	Thr	Xaa	Pro	Asn	Ile	Tyr	Asp	Tyr	Asn	Tyr	Met
								210	215	220					

Gln	Gln	Glu	Ala	Gly	Lys	Val	His	Lys	Ser	Ala	Phe	Gly	Lys	Glu
								225	230	235	240			

Val	Ile	Tyr	Gly	Asn	Asn	Gly	Gly	Lys	Arg	Ser	Leu	Asp	Lys	Thr	Tyr
								245	250	255					

Leu	Ala	Asp	Ala	Leu	Gly	Thr	Gly	Lys	Val	Thr	Leu	Lys	Tyr	Leu	His
								260	265	270					

Arg	Val	Asp	Ala	Ile	Thr	Gln	Asn	Ser	Gln	Gly	Leu	Tyr	Gln	Ile	Asp
								275	280	285					

Val	Ser	Glu	Ile	Asn	Thr	Ser	Gly	Ala	Thr	Val	Ala	Lys	Lys	Thr	Phe
								290	295	300					

Thr	Cys	Lys	His	Leu	Phe	Met	Cys	Ala	Gly	Ser	Val	Gly	Ser	Thr	Glu
								305	310	315	320				

Met	Leu	Val	Arg	Ala	Arg	Glu	Thr	Gly	Lys	Leu	Pro	Ser	Leu	Pro	Ser
								325	330	335					

Glu	Val	Gly	Thr	His	Trp	Gly	Asn	Asn	Gly	Asn	Val	Met	Thr	Ala	Arg
								340	345	350					

Ala Asn His Met Trp His Pro Thr Gly Thr Lys Gln Ser Thr Ile Pro

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355

360

365

Ala Met Gly Ile Asn Asp Trp Asp Asn Ala Ser Asn Pro Val Xaa Ala
 370 375 380

Glu Ile Ala Pro Leu Pro Thr Gly Phe Glu Thr Trp Ile Ser Leu Tyr
 385 390 395 400

Leu Ala Ile Thr Lys Asn Pro Glu Arg Gly His Phe Glu Tyr Asp Ala
 405 410 415

Thr Lys Gln Gln Ala Val Leu Arg Trp Gly Ala His Gln Ser Gln Pro
 420 425 430

Ser Ile Asn Ser Ala Lys Ala Met Phe Asp Lys Ile Asn Lys Ala Asn
 435 440 445

Thr Thr Ile Tyr Arg Tyr Asp Leu Phe Gly Asn Asn Lys Ala Phe Ala
 450 455 460

Asp Asp Phe Thr Tyr His Pro Leu Gly Gly Cys Val Leu Gly Lys Ala
 465 470 475 480

Thr Asp Leu Tyr Gly Arg Ile Lys Gly Tyr Ser Asn Leu Tyr Val Asn
 485 490 495

Asp Gly Ala Leu Val Pro Gly Asn Thr Gly Val Asn Pro Phe Ile Thr
 500 505 510

Ile Thr Ala Met Ala Glu Arg Asn Ile Glu Lys Ile Ile Gln Glu Asp
 515 520 525

Met Leu Lys
 530

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<210> SEQ_ID NO 24
<211> LENGTH: 541
<212> TYPE: PRT
<213> ORGANISM: Kribbella flavaida
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (157)..(157)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
  Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (226)..(226)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
  Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (393)..(393)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
  or Asp, provided that when Xaa157 is Met, then Xaa393 is not Phe
```

<400> SEQUENCE: 24

Met Thr Ala Ser Asn Glu Thr Asn Gln Ser Val Val Thr Arg Arg Arg
 1 5 10 15

Phe Ala Gly Leu Ala Ala Phe Thr Ser Ala Ala Ala Leu Gly Leu Ser
 20 25 30

Arg Val Gly Asp Ala Val Ala Ala Glu Arg Ser Phe Val Pro Ala Val
 35 40 45

Val Val Gly Thr Gly Tyr Gly Ala Ala Val Thr Ala Leu Arg Leu Gly
 50 55 60

Glu Ala Gly Val Ala Thr Thr Met Leu Glu Met Gly Gln Pro Trp Asn
 65 70 75 80

Gln Pro Gly Ala Asp Gly Lys Val Phe Cys Ser Thr Leu Ala Pro Asp
 85 90 95

Arg Arg Ser Met Trp Phe His Arg Arg Thr Ala Ala Pro Leu Asp Thr
 100 105 110

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Phe Leu Trp Leu Asp Val Val Asn Arg Asp Leu Gly Thr Pro Tyr Ala
115 120 125

Gly Val Leu Asp Arg Ile Asp Phe Pro Ala Met Asp Val Tyr Val Gly
130 135 140

Arg Gly Val Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Pro Thr
145 150 155 160

Pro Arg Arg Ser Tyr Phe Glu Gln Val Leu Pro Arg Val Asp Ala Asp
165 170 175

Gln Met Tyr Arg Arg Trp Phe Pro Leu Ala Asn Arg Met Leu Gly Val
180 185 190

Asn Ser Ile Asp Pro Arg Tyr Leu Glu Thr Thr Pro Ala Tyr Arg Tyr
195 200 205

Ala Arg Val Ser Arg Arg His Ala His Gln Ala Gly Phe Arg Thr Ala
210 215 220

Val Xaa Pro Asn Val Tyr Asp Phe Gly Tyr Leu Glu Gln Glu Glu Arg
225 230 235 240

Arg Gln Val Pro Arg Ser Ala Leu Ala Gly Glu Val Ile Tyr Gly Asn
245 250 255

Asn His Gly Lys Gln Ser Leu Asp Lys Thr Tyr Leu Ala Asp Ala Val
260 265 270

Gly Thr Gly Arg Val Thr Ile Arg Thr Leu Thr Arg Val Val Ser Val
275 280 285

Arg Ala Asp Arg Arg Gly Tyr Val Leu Gly Leu Glu Gln Ile Asp Ala
290 295 300

Ser Gly Lys Val Val Arg Arg Ser Glu Leu Gly Cys Arg Gln Leu Phe
305 310 315 320

Leu Gly Ala Gly Ser Ile Gly Thr Thr Glu Leu Leu Leu Arg Ala Arg
325 330 335

Glu Thr Gly Thr Leu Pro Asp Leu Pro Asp Ala Ile Gly Glu Gly Trp
340 345 350

Gly Thr Asn Gly Asn Val Met Thr Ala Arg Ala Asn His Ala Trp Asp
355 360 365

Pro Thr Gly Ser Leu Gln Ser Thr Ile Pro Ala Val Ala Ile Asp Asn
370 375 380

Trp Asp Asp Pro Val His Pro Ala Xaa Ala Glu Ile Ala Pro Leu Pro
385 390 395 400

Thr Gly Leu Glu Thr Trp Ala Gly Leu Tyr Leu Ala Ile Thr Ala Asn
405 410 415

Pro Glu Arg Gly Arg Leu Ser Tyr Asp His Ala Thr Asp Arg Ala Ile
420 425 430

Leu His Trp Gln Ala Ser Gln Ser Thr Pro Ser Ile Gln Ala Ala Lys
435 440 445

Ala Leu Phe Asp Arg Ile Asn Arg Ala Thr Gly Thr Thr Tyr Arg Arg
450 455 460

Asp Leu Phe Ser Gly Asn Arg Ala Phe Ala Ala Asp Phe Cys Tyr His
465 470 475 480

Pro Leu Gly Gly Cys Val Leu Gly Arg Ala Thr Asp Asp Tyr Gly Arg
485 490 495

Val Arg Gly His Arg Asn Leu Tyr Val Thr Asp Ser Ala Leu Leu Pro
500 505 510

Gly Ser Ile Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu
515 520 525

Arg Asn Ile Ala Arg Val Ile Ala Thr Asp Leu Thr Arg

530	535	540
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<210> SEQ_ID NO 25
 <211> LENGTH: 543
 <212> TYPE: PRT
 <213> ORGANISM: Streptomyces sviceus
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (159)..(159)
 <223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
 Tyr, Lys or Ser
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (228)..(228)
 <223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (396)..(396)
 <223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa159 is Met, then Xaa396 is not Phe

 <400> SEQUENCE: 25

Met Ala Thr Lys Leu Ile Gln Arg Gln Leu Thr Arg Arg Gln Ile Leu
 1 5 10 15

Gly Met Ala Ala Leu Gln Thr Ala Ala Thr Leu Gly Phe Thr Arg Val
 20 25 30

Gly Leu Gln Ser Ala Arg Ala Asp Glu Pro Ala Ala Val Glu Ser Ala
 35 40 45

Pro Ala Ile Val Val Gly Ser Gly Tyr Gly Ala Ser Val Ala Ala Leu
 50 55 60

Arg Leu Gly Gln Ala Gly Ile Arg Thr Leu Val Leu Glu Met Gly Arg
 65 70 75 80

Leu Trp Asn Thr Ala Gly Pro Asp Gly Lys Val Phe Cys Asn Thr Ala
 85 90 95

Asn Pro Asp Gln Arg Ser Met Trp Phe Arg Thr Arg Thr Glu Ala Pro
 100 105 110

Leu Ala Thr Phe Leu Trp Leu Asp Val Val Asn Lys Asp Val Ser Pro
 115 120 125

Tyr Pro Gly Val Leu Asp Arg Val His Phe Asp His Met Ser Val Phe
 130 135 140

Val Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly Ser Xaa Ala
 145 150 155 160

Val Thr Pro Leu Gln Ser Tyr Phe Ala Glu Gln Phe Pro Thr Val Asp
 165 170 175

Thr Ala Glu Met Tyr Gly Thr Tyr Phe Pro Arg Ala Arg Ala Met Leu
 180 185 190

Gly Val Asn Thr Ile Asp Pro Ala Trp Phe Glu Ser Thr Glu Trp Tyr
 195 200 205

Lys Phe Thr Arg Val Ser Arg Lys His Ala Gln Asn Thr Gly Leu Lys
 210 215 220

Thr Thr Phe Xaa Pro Ser Val Tyr Asp Phe Gly Tyr Met Gln Arg Glu
 225 230 235 240

Ala Ala Gly Thr Ala Thr Lys Ser Ala Leu Gly Gln Glu Val Ile Tyr
 245 250 255

Gly Asn Asn Phe Gly Lys Lys Ser Leu Asp Lys Thr Tyr Leu Ala Ser
 260 265 270

Ala Leu Gly Thr Gly Asn Val Thr Ile His Thr Met Glu Lys Val Thr
 275 280 285

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Gly Ile Ser Arg Ala Gly Asp Gly Ser Trp Val Leu Ser Ala Glu Arg
290 295 300

Ile Asp Tyr Ser Gly Ala Val Val Glu Thr Lys Gln Tyr Ser Cys Thr
305 310 315 320

Tyr Leu Phe Leu Gly Gly Ser Leu Gly Thr Ser Glu Leu Leu Leu
325 330 335

Arg Ser Arg Gln Ser Gly Thr Leu Pro Ala Leu Asp Ala Ser Val Gly
340 345 350

Ala Gly Trp Gly Pro Asn Gly Asn Thr Met Leu Gly Arg Ala Asn His
355 360 365

Leu Trp Asp Thr Val Gly Ala Asn Gln Ser Thr Met Pro Val Met Gly
370 375 380

Ile Asp Asp Trp Ala Asn Thr Asp Asn Pro Val Xaa Ala Glu Ile Ala
385 390 395 400

Pro Leu Pro Thr Gly Leu Glu His Trp Val Ser Leu Tyr Leu Ala Ile
405 410 415

Thr Lys Asn Pro Gln Arg Ala Arg Phe Ser Tyr Gly Ser Gly Gly Leu
420 425 430

Ser Leu Asp Trp Ser Gly Ala Gln Ser Ala Val Ser Ser Gly Met Ala
435 440 445

Lys Lys Leu Phe Asp Arg Ile Asn Ser Ala Asn Ser Thr Ile Tyr Arg
450 455 460

Tyr Asp Leu Phe Gly Ser Pro Ser Arg Val Phe Ala Asp Asp Phe Thr
465 470 475 480

Tyr His Pro Leu Gly Gly Cys Val Leu Gly Lys Ala Thr Asp Asn Tyr
485 490 495

Gly Arg Val Lys Gly Tyr Ser Arg Leu Tyr Val Thr Asp Gly Ser Leu
500 505 510

Ile Pro Gly Asn Ile Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu
515 520 525

Ala Glu Arg Thr Met Ala Arg Val Leu Val Glu Asp Thr Ala Pro
530 535 540

<210> SEQ ID NO 26
<211> LENGTH: 534
<212> TYPE: PRT
<213> ORGANISM: Saccharomonospora viridis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (150)..(150)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (219)..(219)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (387)..(387)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa150 is Met, then Xaa387 is not Phe

<400> SEQUENCE: 26

Met Arg Pro Leu Ser Arg Arg Arg Leu Leu Gly Leu Leu Ala Val Asn
1 5 10 15

Thr Ala Ser Ala Leu Gly Leu Gly Thr Ile Ala Thr Pro Ser Ala Ala
20 25 30

Ala Ala Ser Arg Arg Asp Phe Ser Pro Ala Val Val Val Gly Thr Gly
35 40 45

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Tyr Gly Ala Ala Val Thr Ala Leu Arg Leu Gly Gln Ala Gly Ile Pro
50 55 60

Thr Val Met Leu Glu Met Gly Arg Leu Trp Asp Thr Pro Gly Asp Asp
65 70 75 80

Gly Arg Val Phe Cys Asp Met Leu Asn Pro Asp Arg Arg Ala Met Trp
85 90 95

Leu Ala Thr Arg Thr Gln Met Pro Leu Ser Ser Phe Leu Trp Leu Asp
100 105 110

Ile Asp Arg Arg Ile Glu Arg Phe Thr Gly Val Leu Asp Cys Val His
115 120 125

His Gly Asp Ile Ser Val Tyr Val Gly Arg Gly Val Gly Gly Ser
130 135 140

Leu Val Asn Gly Ala Xaa Ala Val Thr Pro Lys Arg Ala Thr Phe Ala
145 150 155 160

Glu Ala Phe Pro Asp Val Asp Ser Asp Gly Met Tyr Arg Thr Tyr Phe
165 170 175

Pro Arg Ala Ala Ala Met Leu Gly Val Asn His Ile Asp Pro Ala Trp
180 185 190

Phe Glu Thr Cys Glu Ser Tyr Arg Tyr Ala Arg Val Ser Arg Ala His
195 200 205

Ala His Asn Ala Gly Leu Thr Thr Phe Xaa Pro Ser Val Tyr Asp
210 215 220

Phe Ala Arg Met Arg Arg Glu Glu Ala Gly Glu Val Pro Arg Ser Ala
225 230 235 240

Leu Ala Ala Glu Val Ile Tyr Gly Asn Asn His Gly Lys Arg Ser Leu
245 250 255

Asp Lys Thr Tyr Leu Ala Asp Ala Leu Gly Thr Gly Cys Val Ser Ile
260 265 270

Arg Thr Leu His His Val Arg Ala Ile Glu Gln Asp Ala Asp Gly Thr
275 280 285

Tyr Val Leu Thr Val Asp Glu Leu Asp Leu Asp Gly Thr Arg Val Ala
290 295 300

Thr Arg Gln Leu Gly Ala Arg Tyr Leu Phe Leu Gly Ala Gly Ser Leu
305 310 315 320

Gly Ser Thr Glu Leu Leu Leu Arg Ala Arg Asp Thr Gly Ala Leu Pro
325 330 335

Gly Leu Ser Pro Leu Ile Gly Arg Asp Trp Gly Pro Asn Gly Asn Val
340 345 350

Met Val Gly Arg Ala Asn Arg Pro Arg Asp Arg Thr Gly Thr Val Gln
355 360 365

Ser Gly Met Pro Ala Leu Gly Ile Asp Ala Trp Asp Asp Pro Arg His
370 375 380

Pro Val Xaa Ala Glu Val Ala Pro Met Pro Ala Gly Val Glu Leu Trp
385 390 395 400

Val Ser Leu Tyr Leu Ala Val Thr Arg Asn Pro Glu Arg Gly Leu Leu
405 410 415

Thr Tyr Asp Ala Gly Ser Asp Arg Val Arg Leu His Trp Leu Ser Gly
420 425 430

Gln Ala Gln Pro Ser Val Asp Gln Ala Lys Ala Leu Phe Asp Arg Leu
435 440 445

Asn Ala Ala Asn Gly Thr Glu Tyr Arg Ser Asp Leu Phe Gly Asp Thr
450 455 460

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Arg Val Phe Glu Thr Arg Leu Thr Tyr His Pro Leu Gly Gly Ala Val
465 470 475 480

Leu Gly Lys Ala Thr Asp Ala Tyr Gly Arg Val Arg Gly Gln Arg Arg
485 490 495

Leu Tyr Val Thr Asp Gly Ser Leu Val Pro Gly Asn Ile Gly Val Asn
500 505 510

Pro Phe Leu Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg Ile
515 520 525

Leu Ala Glu Asp Leu Arg
530

<210> SEQ ID NO 27
<211> LENGTH: 552
<212> TYPE: PRT
<213> ORGANISM: Rhodococcus equi
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (167)..(167)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (236)..(236)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (404)..(404)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa167 is Met, then Xaa404 is not Phe
<400> SEQUENCE: 27

Met Thr Asp Ser Arg Ala Asn Arg Ala Asp Ala Thr Arg Gly Val Ala
1 5 10 15

Ser Val Ser Arg Arg Arg Phe Leu Ala Gly Ala Gly Leu Thr Ala Gly
20 25 30

Ala Ile Ala Leu Ser Ser Met Ser Thr Ser Ala Ser Ala Ala Pro Ser
35 40 45

Arg Thr Leu Ala Asp Gly Asp Arg Val Pro Ala Leu Val Ile Gly Ser
50 55 60

Gly Tyr Gly Gly Ala Val Ala Ala Leu Arg Leu Thr Gln Ala Gly Ile
65 70 75 80

Pro Thr Gln Ile Val Glu Met Gly Arg Ser Trp Asp Thr Pro Gly Ser
85 90 95

Asp Gly Lys Ile Phe Cys Gly Met Leu Asn Pro Asp Lys Arg Ser Met
100 105 110

Trp Leu Ala Asp Lys Thr Asp Gln Pro Val Ser Asn Phe Met Gly Phe
115 120 125

Gly Ile Asn Lys Ser Ile Asp Arg Tyr Val Gly Val Leu Asp Ser Glu
130 135 140

Arg Phe Ser Gly Ile Lys Val Tyr Gln Gly Arg Gly Val Gly Gly
145 150 155 160

Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Asn Tyr Phe
165 170 175

Glu Glu Ile Leu Pro Ser Val Asp Ser Asn Glu Met Tyr Asn Lys Tyr
180 185 190

Phe Pro Arg Ala Asn Thr Gly Leu Gly Val Asn Asn Ile Asp Gln Ala
195 200 205

Trp Phe Glu Ser Thr Glu Trp Tyr Lys Phe Ala Arg Thr Gly Arg Lys
210 215 220

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Thr Ala Gln Arg Ser Gly Phe Thr Thr Ala Phe Xaa Pro Asn Val Tyr
 225 230 235 240
 Asp Phe Glu Tyr Met Lys Lys Glu Ala Ala Gly Gln Val Thr Lys Ser
 245 250 255
 Gly Leu Gly Gly Glu Val Ile Tyr Gly Asn Asn Ala Gly Lys Lys Ser
 260 265 270
 Leu Asp Lys Thr Tyr Leu Ala Gln Ala Ala Ala Thr Gly Lys Leu Thr
 275 280 285
 Ile Thr Thr Leu His Arg Val Thr Lys Val Ala Pro Ala Thr Gly Ser
 290 295 300
 Gly Tyr Ser Val Thr Met Glu Gln Ile Asp Glu Gln Gly Asn Val Val
 305 310 315 320
 Ala Thr Lys Val Val Thr Ala Asp Arg Val Phe Phe Ala Ala Gly Ser
 325 330 335
 Val Gly Thr Ser Lys Leu Leu Val Ser Met Lys Ala Gln Gly His Leu
 340 345 350
 Pro Asn Leu Ser Ser Gln Val Gly Glu Gly Trp Gly Asn Asn Gly Asn
 355 360 365
 Ile Met Val Gly Arg Ala Asn His Met Trp Asp Ala Thr Gly Ser Lys
 370 375 380
 Gln Ala Thr Ile Pro Thr Met Gly Ile Asp Asn Trp Ala Asp Pro Thr
 385 390 395 400
 Ala Pro Ile Xaa Ala Glu Ile Ala Pro Leu Pro Ala Gly Leu Glu Thr
 405 410 415
 Tyr Val Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Ala Arg
 420 425 430
 Phe Gln Phe Asn Ser Gly Thr Gly Lys Val Asp Leu Thr Trp Ala Gln
 435 440 445
 Ser Gln Asn Gln Lys Gly Ile Asp Met Ala Lys Lys Val Phe Asp Lys
 450 455 460
 Ile Asn Gln Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Val
 465 470 475 480
 Tyr Phe Lys Thr Trp Gly Asp Asp Phe Thr Tyr His Pro Leu Gly Gly
 485 490 495
 Val Leu Leu Asn Lys Ala Thr Asp Asn Phe Gly Arg Leu Pro Glu Tyr
 500 505 510
 Pro Gly Leu Tyr Val Val Asp Gly Ser Leu Val Pro Gly Asn Val Gly
 515 520 525
 Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Met Asp
 530 535 540
 Lys Ile Ile Ser Ser Asp Ile Gln
 545 550

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<210> SEQ ID NO 28
<211> LENGTH: 507
<212> TYPE: PRT
<213> ORGANISM: Brevibacterium sterolicum
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (122)..(122)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
   Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (191)..(191)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
   Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
  
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<220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (359) .. (359)
 <223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His or Asp, provided that when Xaa122 is Met, then Xaa359 is not Phe

<400> SEQUENCE: 28

Ala Pro Ser Arg Thr Leu Ala Asp Gly Asp Arg Val Pro Ala Leu Val
 1 5 10 15

Ile Gly Ser Gly Tyr Gly Gly Ala Val Ala Ala Leu Arg Leu Thr Gln
 20 25 30

Ala Gly Ile Pro Thr Gln Ile Val Glu Met Gly Arg Ser Trp Asp Thr
 35 40 45

Pro Gly Ser Asp Gly Lys Ile Phe Cys Gly Met Leu Asn Pro Asp Lys
 50 55 60

Arg Ser Met Trp Leu Ala Asp Lys Thr Asp Gln Pro Val Ser Asn Phe
 65 70 75 80

Met Gly Phe Gly Ile Asn Lys Ser Ile Asp Arg Tyr Val Gly Val Leu
 85 90 95

Asp Ser Glu Arg Phe Ser Gly Ile Lys Val Tyr Gln Gly Arg Gly Val
 100 105 110

Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg
 115 120 125

Asn Tyr Phe Glu Glu Ile Leu Pro Ser Val Asp Ser Asn Glu Met Tyr
 130 135 140

Asn Lys Tyr Phe Pro Arg Ala Asn Thr Gly Leu Gly Val Asn Asn Ile
 145 150 155 160

Asp Gln Ala Trp Phe Glu Ser Thr Glu Trp Tyr Lys Phe Ala Arg Thr
 165 170 175

Gly Arg Lys Thr Ala Gln Arg Ser Gly Phe Thr Thr Ala Phe Xaa Pro
 180 185 190

Asn Val Tyr Asp Phe Glu Tyr Met Lys Lys Glu Ala Ala Gly Gln Val
 195 200 205

Thr Lys Ser Gly Leu Gly Glu Val Ile Tyr Gly Asn Asn Ala Gly
 210 215 220

Lys Lys Ser Leu Asp Lys Thr Tyr Leu Ala Gln Ala Ala Ala Thr Gly
 225 230 235 240

Lys Leu Thr Ile Thr Thr Leu His Arg Val Thr Lys Val Ala Pro Ala
 245 250 255

Thr Gly Ser Gly Tyr Ser Val Thr Met Glu Gln Ile Asp Glu Gln Gly
 260 265 270

Asn Val Val Ala Thr Lys Val Val Thr Ala Asp Arg Val Phe Phe Ala
 275 280 285

Ala Gly Ser Val Gly Thr Ser Lys Leu Leu Val Ser Met Lys Ala Gln
 290 295 300

Gly His Leu Pro Asn Leu Ser Ser Gln Val Gly Glu Gly Trp Gly Asn
 305 310 315 320

Asn Gly Asn Ile Met Val Gly Arg Ala Asn His Met Trp Asp Ala Thr
 325 330 335

Gly Ser Lys Gln Ala Thr Ile Pro Thr Met Gly Ile Asp Asn Trp Ala
 340 345 350

Asp Pro Thr Ala Pro Ile Xaa Ala Glu Ile Ala Pro Leu Pro Ala Gly
 355 360 365

Leu Glu Thr Tyr Val Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro Glu
 370 375 380

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Arg Ala Arg Phe Gln Phe Asn Ser Gly Thr Gly Lys Val Asp Leu Thr
 385 390 395 400

Trp Ala Gln Ser Gln Asn Gln Lys Gly Ile Asp Met Ala Lys Lys Val
 405 410 415

Phe Asp Lys Ile Asn Gln Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu
 420 425 430

Phe Gly Val Tyr Tyr Lys Thr Trp Gly Asp Asp Phe Thr Tyr His Pro
 435 440 445

Leu Gly Gly Val Leu Leu Asn Lys Ala Thr Asp Asn Phe Gly Arg Leu
 450 455 460

Pro Glu Tyr Pro Gly Leu Tyr Val Val Asp Gly Ser Leu Val Pro Gly
 465 470 475 480

Asn Val Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg
 485 490 495

Asn Met Asp Lys Ile Ile Ser Ser Asp Ile Gln
 500 505

<210> SEQ ID NO 29
<211> LENGTH: 552
<212> TYPE: PRT
<213> ORGANISM: *Brevibacterium sterolicum*
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (167)..(167)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
 Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (236)..(236)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (404)..(404)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa167 is Met, then Xaa404 is not Phe

<400> SEQUENCE: 29

Met Thr Asp Ser Arg Ala Asn Arg Ala Asp Ala Thr Arg Gly Val Ala
 1 5 10 15

Ser Val Ser Arg Arg Arg Phe Leu Ala Gly Ala Gly Leu Thr Ala Gly
 20 25 30

Ala Ile Ala Leu Ser Ser Met Ser Thr Ser Ala Ser Ala Ala Pro Ser
 35 40 45

Arg Thr Leu Ala Asp Gly Asp Arg Val Pro Ala Leu Val Ile Gly Ser
 50 55 60

Gly Tyr Gly Gly Ala Val Ala Ala Leu Arg Leu Thr Gln Ala Gly Ile
 65 70 75 80

Pro Thr Gln Ile Val Glu Met Gly Arg Ser Trp Asp Thr Pro Gly Ser
 85 90 95

Asp Gly Lys Ile Phe Cys Gly Met Leu Asn Pro Asp Lys Arg Ser Met
 100 105 110

Trp Leu Ala Asp Lys Thr Asp Gln Pro Val Ser Asn Phe Met Gly Phe
 115 120 125

Gly Ile Asn Lys Ser Ile Asp Arg Tyr Val Gly Val Leu Asp Ser Glu
 130 135 140

Arg Phe Ser Gly Ile Lys Val Tyr Gln Gly Arg Gly Val Gly Gly
 145 150 155 160

Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Asn Tyr Phe

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165	170	175
Glu Glu Ile Leu Pro Ser Val Asp Ser Asn Glu Met Tyr Asn Lys Tyr		
180	185	190
Phe Pro Arg Ala Asn Thr Gly Leu Gly Val Asn Asn Ile Asp Gln Ala		
195	200	205
Trp Phe Glu Ser Thr Glu Trp Tyr Lys Phe Ala Arg Thr Gly Arg Lys		
210	215	220
Thr Ala Gln Arg Ser Gly Phe Thr Thr Ala Phe Xaa Pro Asn Val Tyr		
225	230	235
Asp Phe Glu Tyr Met Lys Lys Glu Ala Ala Gly Gln Val Thr Lys Ser		
245	250	255
Gly Leu Gly Gly Glu Val Ile Tyr Gly Asn Asn Ala Gly Lys Lys Ser		
260	265	270
Leu Asp Lys Thr Tyr Leu Ala Gln Ala Ala Ala Thr Gly Lys Leu Thr		
275	280	285
Ile Thr Thr Leu His Arg Val Thr Lys Val Ala Pro Ala Thr Gly Ser		
290	295	300
Gly Tyr Ser Val Thr Met Glu Gln Ile Asp Glu Gln Gly Asn Val Val		
305	310	315
Ala Thr Lys Val Val Thr Ala Asp Arg Val Phe Phe Ala Ala Gly Ser		
325	330	335
Val Gly Thr Ser Lys Leu Leu Val Ser Met Lys Ala Gln Gly His Leu		
340	345	350
Pro Asn Leu Ser Ser Gln Val Gly Glu Gly Trp Gly Asn Asn Gly Asn		
355	360	365
Ile Met Val Gly Arg Ala Asn His Met Trp Asp Ala Thr Gly Ser Lys		
370	375	380
Gln Ala Thr Ile Pro Thr Met Gly Ile Asp Asn Trp Ala Asp Pro Thr		
385	390	395
Ala Pro Ile Xaa Ala Glu Ile Ala Pro Leu Pro Ala Gly Leu Glu Thr		
405	410	415
Tyr Val Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Ala Arg		
420	425	430
Phe Gln Phe Asn Ser Gly Thr Gly Lys Val Asp Leu Thr Trp Ala Gln		
435	440	445
Ser Gln Asn Gln Lys Gly Ile Asp Met Ala Lys Lys Val Phe Asp Lys		
450	455	460
Ile Asn Gln Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Val		
465	470	475
Tyr Phe Lys Thr Trp Gly Asp Asp Phe Thr Tyr His Pro Leu Gly Gly		
485	490	495
Val Leu Leu Asn Lys Ala Thr Asp Asn Phe Gly Arg Leu Pro Glu Tyr		
500	505	510
Pro Gly Leu Tyr Val Val Asp Gly Ser Leu Val Pro Gly Asn Val Gly		
515	520	525
Val Asn Pro Phe Val Thr Ile Thr Arg Leu Ala Glu Arg Asn Met Asp		
530	535	540
Lys Ile Ile Ser Ser Asp Ile Gln		
545	550	

<210> SEQ ID NO 30

<211> LENGTH: 551

<212> TYPE: PRT

<213> ORGANISM: Rhodococcus equi

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<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (167) ..(167)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
      Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (236) ..(236)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
      Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (404) ..(404)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
      or Asp, provided that when Xaa167 is Met, then Xaa404 is not Phe

<400> SEQUENCE: 30

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Met Thr Asp Ser Arg Ala Asn Arg Ala Asp Ala Thr Arg Gly Val Ala
 1 5 10 15

Ser Val Ser Arg Arg Arg Phe Leu Ala Gly Ala Gly Leu Thr Ala Gly
 20 25 30

Ala Ile Ala Leu Ser Ser Met Ser Thr Ser Ala Ser Ala Ala Pro Ser
 35 40 45

Arg Thr Leu Ala Asp Gly Asp Arg Val Pro Ala Leu Val Ile Gly Ser
 50 55 60

Gly Tyr Gly Gly Ala Val Ala Ala Leu Arg Leu Thr Gln Ala Gly Ile
 65 70 75 80

Pro Thr Gln Ile Val Glu Met Gly Arg Ser Trp Asp Thr Pro Gly Ser
 85 90 95

Asp Gly Lys Ile Phe Cys Gly Met Leu Asn Pro Asp Lys Arg Ser Met
 100 105 110

Trp Leu Ala Asp Lys Thr Asp Gln Pro Val Ser Asn Phe Met Gly Phe
 115 120 125

Gly Ile Asn Lys Ser Ile Asp Arg Tyr Val Gly Val Leu Asp Ser Glu
 130 135 140

Arg Phe Ser Gly Ile Lys Val Tyr Gln Gly Arg Gly Val Gly Gly Gly
 145 150 155 160

Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Asn Tyr Phe
 165 170 175

Glu Glu Ile Leu Pro Ser Val Asp Ser Asn Glu Met Tyr Asn Lys Tyr
 180 185 190

Phe Pro Arg Ala Asn Thr Gly Leu Gly Val Asn Asn Ile Asp Gln Ala
 195 200 205

Trp Phe Glu Ser Thr Glu Trp Tyr Lys Phe Ala Arg Thr Gly Arg Lys
 210 215 220

Thr Ala Gln Arg Ser Gly Phe Thr Thr Ala Phe Xaa Pro Asn Val Tyr
 225 230 235 240

Asp Phe Glu Tyr Met Lys Lys Glu Ala Ala Gly Gln Val Thr Lys Ser
 245 250 255

Gly Leu Gly Gly Glu Val Ile Tyr Gly Asn Asn Ala Gly Lys Lys Ser
 260 265 270

Leu Asp Lys Thr Tyr Leu Ala Gln Ala Ala Ala Thr Gly Lys Leu Thr
 275 280 285

Ile Thr Thr Leu His Arg Val Thr Lys Val Ala Pro Ala Thr Gly Ser
 290 295 300

Gly Tyr Ser Val Thr Met Glu Gln Ile Asp Glu Gln Gly Asn Val Val
 305 310 315 320

Ala Thr Lys Val Val Thr Ala Asp Arg Val Phe Phe Ala Ala Gly Ser

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325	330	335
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Val Gly Thr Ser Lys Leu Leu Val Ser Met Lys Ala Gln Gly His Leu 340	345	350
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Pro Asn Leu Ser Ser Gln Val Gly Glu Gly Trp Gly Asn Asn Gly Asn 355	360	365
--	-----	-----

Ile Met Val Gly Arg Ala Asn His Met Trp Asp Ala Thr Gly Ser Lys 370	375	380
--	-----	-----

Gln Ala Thr Ile Pro Thr Met Gly Ile Asp Asn Trp Ala Asp Pro Thr 385	390	395	400
--	-----	-----	-----

Ala Pro Ile Xaa Ala Glu Ile Ala Pro Leu Pro Ala Gly Leu Glu Thr 405	410	415
--	-----	-----

Tyr Val Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Ala Arg 420	425	430
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Phe Gln Phe Asn Ser Gly Thr Gly Lys Val Asp Leu Thr Trp Ala Gln 435	440	445
--	-----	-----

Ser Gln Asn Gln Lys Gly Ile Asp Met Ala Lys Lys Val Phe Asp Lys 450	455	460
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Ile Asn Gln Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Val 465	470	475	480
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Tyr Lys Thr Trp Gly Asp Asp Phe Thr Tyr His Pro Leu Gly Gly Val 485	490	495
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Leu Leu Asn Lys Ala Thr Asp Asn Phe Gly Arg Leu Pro Glu Tyr Pro 500	505	510
--	-----	-----

Gly Leu Tyr Val Val Asp Gly Ser Leu Val Pro Gly Asn Val Gly Val 515	520	525
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Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Met Asp Lys 530	535	540
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Ile Ile Ser Ser Asp Ile Gln 545	550
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<210> SEQ_ID NO 31
<211> LENGTH: 551
<212> TYPE: PRT
<213> ORGANISM: Brevibacterium sp.
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (167)..(167)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (236)..(236)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (404)..(404)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa167 is Met, then Xaa404 is not Phe

<400> SEQUENCE: 31

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Met Thr Asp Ser Arg Ala Asn Arg Ala Asp Ala Thr Arg Gly Val Ala 1	5	10	15
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Ser Val Ser Arg Arg Arg Phe Leu Ala Gly Ala Gly Leu Thr Ala Gly 20	25	30
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Ala Ile Ala Leu Ser Ser Met Ser Thr Ser Ala Ser Ala Ala Pro Ser 35	40	45
---	----	----

Arg Thr Leu Ala Asp Gly Asp Arg Val Pro Ala Leu Val Ile Gly Ser 50	55	60
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Gly Tyr Gly Gly Ala Val Ala Ala Leu Arg Leu Thr Gln Ala Gly Ile
65 70 75 80

Pro Thr Gln Ile Val Glu Met Gly Arg Ser Trp Asp Thr Pro Gly Ser
85 90 95

Asp Gly Lys Ile Phe Cys Gly Met Leu Asn Pro Asp Lys Arg Ser Met
100 105 110

Arg Leu Ala Asp Lys Thr Asp Gln Pro Val Ser Asn Phe Met Gly Phe
115 120 125

Gly Ile Asn Lys Ser Ile Asp Arg Tyr Val Gly Val Leu Asp Ser Glu
130 135 140

Arg Phe Ser Gly Ile Lys Val Tyr Gln Gly Arg Gly Val Gly Gly
145 150 155 160

Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Asn Tyr Phe
165 170 175

Glu Glu Ile Leu Pro Ser Val Asp Ser Asn Glu Met Tyr Asn Lys Tyr
180 185 190

Phe Pro Arg Ala Asn Thr Gly Leu Gly Val Asn Asn Ile Asp Gln Ala
195 200 205

Trp Phe Glu Ser Thr Glu Trp Tyr Lys Phe Ala Arg Thr Gly Arg Lys
210 215 220

Thr Ala Gln Arg Ser Gly Phe Thr Thr Ala Phe Xaa Pro Asn Val Tyr
225 230 235 240

Asp Phe Glu Tyr Met Lys Lys Glu Ala Ala Gly Gln Val Thr Lys Ser
245 250 255

Gly Leu Gly Gly Glu Val Ile Tyr Gly Asn Asn Ala Gly Lys Lys Ser
260 265 270

Leu Asp Lys Thr Tyr Leu Ala Gln Ala Ala Ala Thr Gly Lys Leu Thr
275 280 285

Ile Thr Thr Leu His Arg Val Thr Lys Val Ala Pro Ala Thr Gly Ser
290 295 300

Gly Tyr Ser Val Thr Met Glu Gln Ile Asp Glu Gln Gly Asn Val Val
305 310 315 320

Ala Thr Lys Val Val Thr Ala Asp Arg Val Phe Phe Ala Ala Gly Ser
325 330 335

Val Gly Thr Ser Lys Leu Leu Val Ser Met Lys Ala Gln Gly His Leu
340 345 350

Pro Asn Leu Ser Ser Gln Val Gly Glu Gly Trp Gly Asn Asn Gly Asn
355 360 365

Ile Met Val Gly Arg Ala Asn His Met Trp Asp Ala Thr Gly Ser Lys
370 375 380

Gln Ala Thr Ile Pro Thr Met Gly Ile Asp Asn Trp Ala Asp Pro Ala
385 390 395 400

Ala Pro Ile Xaa Ala Glu Ile Ala Pro Leu Pro Ala Gly Leu Glu Thr
405 410 415

Tyr Val Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Ala Arg
420 425 430

Phe Gln Phe Asn Ser Gly Thr Gly Lys Val Asp Leu Thr Trp Ala Gln
435 440 445

Ser Gln Asn Gln Lys Gly Ile Asp Met Ala Lys Lys Val Phe Asp Lys
450 455 460

Ile Asn Gln Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Val
465 470 475 480

Tyr Lys Thr Trp Gly Asp Asp Phe Thr Tyr His Pro Leu Gly Gly Val

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485	490	495
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Leu Leu Asn Lys Ala Thr Asp Asn Phe Gly Arg Leu Pro Glu Tyr Pro
500 505 510

Gly Leu Tyr Val Val Asp Gly Ser Leu Val Pro Gly Asn Val Gly Val
515 520 525

Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Met Asp Lys
530 535 540

Ile Ile Ser Ser Asp Ile Gln
545 550

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<210> SEQ_ID NO 32
<211> LENGTH: 551
<212> TYPE: PRT
<213> ORGANISM: Rhodococcus sp.
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (167) ..(167)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (236) ..(236)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (405) ..(405)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa167 is Met, then Xaa405 is not Phe
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<400> SEQUENCE: 32

Met Thr Asp Ser Arg Ala Asn Arg Ala Asp Ala Thr Arg Gly Val Ala
1 5 10 15

Ser Val Ser Arg Arg Arg Phe Leu Ala Gly Ala Gly Leu Thr Ala Gly
20 25 30

Ala Ile Ala Leu Ser Ser Met Ser Thr Ser Ala Ser Ala Ala Pro Ser
35 40 45

Arg Thr Leu Ala Asp Gly Asp Arg Val Pro Ala Leu Val Ile Gly Ser
50 55 60

Gly Tyr Gly Gly Ala Val Ala Ala Leu Arg Leu Thr Gln Ala Gly Ile
65 70 75 80

Pro Thr Gln Ile Val Glu Met Gly Arg Ser Trp Asp Thr Pro Gly Ser
85 90 95

Asp Gly Lys Ile Phe Cys Gly Met Leu Asn Pro Asp Lys Arg Ser Met
100 105 110

Trp Leu Ala Asp Lys Thr Asp Gln Pro Val Ser Asn Phe Met Gly Phe
115 120 125

Gly Ile Asn Lys Ser Ile Asp Arg Tyr Val Gly Val Leu Asp Ser Glu
130 135 140

Arg Phe Ser Gly Ile Lys Val Tyr Gln Gly Arg Gly Val Gly Gly Gly
145 150 155 160

Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Asn Tyr Phe
165 170 175

Glu Glu Ile Leu Pro Ser Val Asp Ser Asn Glu Met Tyr Asn Lys Tyr
180 185 190

Phe Pro Arg Ala Asn Thr Gly Leu Gly Val Asn His Ile Asp Gln Ala
195 200 205

Trp Phe Glu Ser Thr Glu Trp Tyr Lys Phe Ala Arg Thr Gly Arg Lys
210 215 220

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Thr Ala Gln Arg Ser Gly Phe Thr Thr Ala Phe Xaa Pro Asn Val Tyr
225 230 235 240

Asp Phe Glu Tyr Met Lys Lys Glu Ala Ala Gly Gln Val Thr Lys Ser
245 250 255

Gly Leu Gly Gly Glu Val Ile Tyr Gly Asn Asn Ala Gly Lys Lys Ser
260 265 270

Leu Asp Lys Thr Tyr Leu Ala Gln Ala Ala Ala Thr Gly Lys Leu Thr
275 280 285

Ile Thr Thr Leu His Arg Val Thr Lys Val Ala Pro Ala Thr Gly Ser
290 295 300

Gly Tyr Ser Val Thr Met Glu Gln Ile Asp Glu Gln Gly Asn Val Val
305 310 315 320

Ala Ala Thr Lys Val Val Thr Ala Asp Arg Val Phe Phe Ala Ala Gly
325 330 335

Ser Val Gly Thr Ser Lys Leu Leu Val Ser Met Lys Ala Gln Gly His
340 345 350

Leu Pro Asn Leu Ser Ser Gln Val Gly Glu Gly Trp Gly Asn Asn Gly
355 360 365

Asn Ile Met Val Gly Arg Ala Asn His Met Trp Asp Ala Thr Gly Ser
370 375 380

Lys Gln Ala Thr Ile Pro Thr Met Gly Ile Asp Asn Trp Ala Asp Pro
385 390 395 400

Thr Ala Pro Ile Xaa Ala Glu Ile Ala Pro Leu Pro Ala Gly Leu Glu
405 410 415

Thr Tyr Val Ser Leu Tyr Leu Ala Ile Thr Lys Asn Pro Glu Arg Ala
420 425 430

Arg Phe Gln Phe Asn Ser Gly Thr Gly Lys Val Asp Leu Thr Trp Ala
435 440 445

Gln Ser Gln Asn Gln Lys Gly Ile Asp Met Ala Lys Lys Val Phe Asp
450 455 460

Lys Ile Asn Gln Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly
465 470 475 480

Val Tyr Lys Thr Trp Gly Asp Asp Phe Thr Tyr His Pro Leu Gly Gly
485 490 495

Val Leu Leu Asn Lys Ala Thr Asp Asn Phe Gly Arg Leu Pro Glu Tyr
500 505 510

Pro Gly Leu Tyr Val Val Asp Gly Ser Leu Val Pro Gly Asn Val Gly
515 520 525

Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Arg Asn Met Asp Lys
530 535 540

Ile Ile Ser Ser Asp Ile Gln
545 550

<210> SEQ_ID NO 33

<211> LENGTH: 533

<212> TYPE: PRT

<213> ORGANISM: Rhodococcus sp.

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (1)..(1)

<223> OTHER INFORMATION: Xaa is unknown

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (158)..(158)

<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

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<222> LOCATION: (227) .. (227)
 <223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (395) .. (395)
 <223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa158 is Met, then Xaa395 is not Phe

<400> SEQUENCE: 33

Xaa	Ala	Thr	Arg	Gly	Val	Ala	Ser	Val	Ser	Arg	Arg	Arg	Phe	Leu	Ala
1				5			10			15					

Gly	Ala	Gly	Leu	Thr	Ala	Gly	Ala	Ile	Ala	Leu	Ser	Ser	Met	Ser	Thr
			20				25			30					

Ser	Ala	Ser	Ala	Ala	Pro	Ser	Arg	Thr	Leu	Ala	Asp	Gly	Asp	Arg	Val
					35		40			45					

Pro	Ala	Leu	Val	Ile	Gly	Ser	Gly	Tyr	Gly	Ala	Val	Ala	Ala	Leu	
			50		55			60							

Arg	Leu	Thr	Gln	Ala	Gly	Ile	Pro	Thr	Gln	Ile	Val	Glu	Met	Gly	Arg
65					70			75			80				

Ser	Trp	Asp	Thr	Pro	Gly	Ser	Asp	Gly	Lys	Ile	Phe	Cys	Gly	Met	Leu
					85			90			95				

Asn	Pro	Asp	Lys	Arg	Ser	Met	Trp	Leu	Ala	Asp	Lys	Thr	Asp	Gln	Pro
					100			105			110				

Val	Ser	Asn	Phe	Met	Gly	Phe	Gly	Ile	Asn	Lys	Ser	Ile	Asp	Arg	Tyr
					115		120			125					

Val	Gly	Val	Leu	Asp	Ser	Glu	Arg	Phe	Ser	Gly	Ile	Lys	Val	Tyr	Gln
					130		135			140					

Gly	Arg	Gly	Val	Gly	Gly	Ser	Leu	Val	Asn	Gly	Gly	Xaa	Ala	Val	
145				150			155			160					

Thr	Pro	Lys	Arg	Asn	Tyr	Phe	Glu	Ile	Leu	Pro	Ser	Val	Asp	Ser	
					165		170			175					

Asn	Glu	Met	Tyr	Asn	Lys	Tyr	Phe	Pro	Arg	Ala	Asn	Thr	Gly	Leu	Gly
					180		185			190					

Val	Asn	Asn	Ile	Asp	Gln	Ala	Trp	Phe	Glu	Ser	Thr	Glu	Trp	Tyr	Lys
					195		200			205					

Phe	Ala	Arg	Thr	Gly	Arg	Lys	Thr	Ala	Gln	Arg	Ser	Gly	Phe	Thr	Thr
					210		215			220					

Ala	Phe	Xaa	Pro	Asn	Val	Tyr	Asp	Phe	Glu	Tyr	Met	Lys	Glu	Ala	
225					230			235			240				

Ala	Gly	Gln	Val	Thr	Lys	Ser	Gly	Leu	Gly	Gly	Glu	Val	Ile	Tyr	Gly
					245		250			255					

Asn	Asn	Ala	Gly	Lys	Lys	Ser	Leu	Asp	Lys	Thr	Tyr	Leu	Ala	Gln	Ala
					260		265			270					

Ala	Ala	Thr	Gly	Lys	Leu	Thr	Ile	Thr	Leu	His	Arg	Val	Thr	Lys	
					275		280			285					

Val	Ala	Pro	Ala	Thr	Gly	Ser	Gly	Tyr	Ser	Val	Thr	Met	Glu	Gln	Ile
					290		295			300					

Asp	Glu	Gln	Gly	Asn	Val	Val	Ala	Thr	Lys	Val	Val	Thr	Ala	Asp	Arg
305					310			315			320				

Val	Phe	Phe	Ala	Ala	Gly	Ser	Val	Gly	Thr	Ser	Lys	Leu	Leu	Val	Ser
					325		330			335					

Met	Lys	Ala	Gln	Gly	His	Leu	Pro	Asn	Leu	Ser	Ser	Gln	Val	Gly	Glu
					340		345			350					

Gly	Trp	Gly	Asn	Asn	Gly	Asn	Ile	Met	Val	Gly	Arg	Ala	Asn	His	Met
					355		360			365					

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Trp Asp Ala Thr Gly Ser Lys Gln Ala Thr Ile Pro Thr Met Gly Ile
370 375 380

Asp Asn Trp Ala Asp Pro Thr Ala Pro Ile Xaa Ala Glu Ile Ala Pro
385 390 395 400

Leu Pro Ala Gly Leu Glu Thr Tyr Val Ser Leu Tyr Leu Ala Ile Thr
405 410 415

Lys Asn Pro Glu Arg Ala Arg Phe Gln Phe Asn Ser Gly Thr Gly Lys
420 425 430

Val Asp Leu Thr Trp Ala Gln Ser Gln Asn Gln Lys Gly Ile Asp Met
435 440 445

Ala Lys Lys Val Phe Asp Lys Ile Asn Gln Lys Glu Gly Thr Ile Tyr
450 455 460

Arg Thr Asp Leu Phe Gly Val Tyr Lys Thr Trp Gly Asp Asp Phe Thr
465 470 475 480

Tyr His Pro Leu Gly Gly Val Leu Leu Asn Lys Ala Thr Asp Asn Phe
485 490 495

Gly Arg Leu Pro Glu Tyr Pro Gly Leu Tyr Val Val Asp Gly Ser Leu
500 505 510

Val Pro Gly Asn Val Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu
515 520 525

Ala Glu Arg Asn Met
530

<210> SEQ_ID NO 34
<211> LENGTH: 552
<212> TYPE: PRT
<213> ORGANISM: Rhodococcus erythropolis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (167)..(167)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (236)..(236)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (405)..(405)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa167 is Met, then Xaa405 is not Phe

<400> SEQUENCE: 34
Met Ser Ile Arg Ala Gly Ser Asn Glu Arg His Ala Arg Thr Asn Ser
1 5 10 15

Thr Leu Ser Arg Arg Asn Phe Leu Ala Ala Thr Gly Leu Ala Val Gly
20 25 30

Ala Ala Ala Leu Ser Ser Ser Trp Thr Thr Ala Ala Ala Ala Pro Arg
35 40 45

Arg Ala Leu Ser Asp Gly Asp Arg Val Pro Ala Leu Val Ile Gly Ser
50 55 60

Gly Tyr Gly Gly Ala Val Ala Ala Leu Arg Leu Thr Gln Ala Gly Ile
65 70 75 80

Asp Thr His Met Val Glu Met Gly Lys Ser Trp Thr Thr Pro Gly Ser
85 90 95

Asp Gly Lys Val Phe Cys Pro Met Leu Ser Pro Asp Gly Arg Ser Phe
100 105 110

Trp Leu Arg Asp Arg Thr Val Gln Pro Val Ser His Phe Ser Gly Gly

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115	120	125
Ser Val Asp Lys Asn Ile Ser Arg Tyr Val Gly Val Leu Asp Ala Glu		
130	135	140
Asp Phe Gly Gly Ile Lys Val Tyr Gln Gly Arg Gly Val Gly Gly		
145	150	155
160		
Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Asn Tyr Phe		
165	170	175
Glu Glu Ile Leu Pro Gly Val Asp Ser Asn Glu Met Tyr Ser Thr Tyr		
180	185	190
Phe Pro Arg Ala Asn Ala Ala Leu Gly Val Asn Asn Ile Asp Pro Ala		
195	200	205
Trp Phe Glu Ser Thr Glu Tyr Tyr Lys Phe Ala Arg Thr Gly Arg Lys		
210	215	220
Thr Ala Glu Arg Ser Gly Tyr Thr Thr Phe Xaa Pro Asn Val Tyr		
225	230	235
240		
Asp Phe Asn Tyr Met Lys Gln Glu Ala Ala Gly Gln Val Thr Lys Ser		
245	250	255
Ala Leu Val Ser Glu Val Ile Tyr Gly Asn Asn Ala Gly Lys Lys Ser		
260	265	270
Leu Asp Lys Thr Tyr Leu Ala Ala Ala Ser Ala Thr Gly Lys Leu Thr		
275	280	285
Ile Ser Ala Leu His Val Val Thr Ser Val Ala Pro Ala Ala Thr Gly		
290	295	300
Gly Gly Tyr Gln Val Val Met Asn Gln Ile Asn Glu Gln Gly Asn Thr		
305	310	315
320		
Val Gly Thr Lys Thr Val Thr Ala Asp Lys Val Phe Phe Ala Ala Gly		
325	330	335
Ser Ile Gly Thr Ser Lys Leu Leu Val Ala Met Lys Ala Gln Gly Gln		
340	345	350
Leu Ala Asn Leu Pro Gly Ala Val Gly Gln Glu Trp Gly His Asn Gly		
355	360	365
Asn Val Met Val Gly Arg Ala Asn His Met Trp Asp Ala Thr Gly Ala		
370	375	380
Lys Gln Ser Ala Ile Pro Val Met Gly Ile Asp Asn Trp Ala Asp Thr		
385	390	395
400		
Ser Ala Pro Val Xaa Ala Glu Ile Ala Pro Phe Pro Ala Gly Thr Glu		
405	410	415
Leu Trp Val Ser Leu Tyr Leu Ala Ile Ala Lys Asn Pro Gln Arg Ala		
420	425	430
Gln Phe Gln Phe Asn Ser Ala Thr Gly Lys Val Gly Leu Asn Trp Gln		
435	440	445
Arg Ser Gln Asn Gln Pro Ser Ile Asp Met Ala Lys Lys Leu Phe Asp		
450	455	460
Lys Ile Asn Lys Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly		
465	470	475
480		
Pro Val Gln Thr Trp Gly Asp Gln Leu Thr Tyr His Pro Leu Gly Gly		
485	490	495
Cys Val Leu Gly Lys Ala Thr Asp Gly Tyr Gly Arg Leu Pro Glu Tyr		
500	505	510
Pro Gly Leu Tyr Val Met Asp Gly Ser Leu Val Pro Gly Asn Val Gly		
515	520	525
Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu		
530	535	540

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Asn Ile Ile Ala Asn Asp Met Asn
545 550

<210> SEQ ID NO 35
<211> LENGTH: 522
<212> TYPE: PRT
<213> ORGANISM: Rhodococcus erythropolis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (137)..(137)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (206)..(206)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (375)..(375)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa137 is Met, then Xaa375 is not Phe

<400> SEQUENCE: 35

Met Gly Ala Ala Ala Leu Ser Ser Ser Trp Thr Thr Ala Ala Ala Ala
1 5 10 15

Pro Arg Arg Ala Leu Asn Asp Gly Asp Arg Val Pro Ala Leu Val Ile
20 25 30

Gly Ser Gly Tyr Gly Gly Ala Val Ala Ala Leu Arg Leu Thr Gln Ala
35 40 45

Gly Ile Asp Thr His Met Val Glu Met Gly Lys Ser Trp Thr Thr Pro
50 55 60

Gly Ser Asp Gly Lys Val Phe Cys Pro Met Leu Ser Pro Asp Gly Arg
65 70 75 80

Ser Phe Trp Leu Arg Asp Arg Thr Val Gln Pro Val Ser His Phe Ser
85 90 95

Gly Gly Ser Val Asp Lys Asn Ile Ser Arg Tyr Val Gly Val Leu Asp
100 105 110

Ala Glu Asp Phe Gly Gly Ile Lys Val Tyr Gln Gly Arg Gly Val Gly
115 120 125

Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Asn
130 135 140

Tyr Phe Glu Glu Ile Leu Pro Gly Val Asp Ser Asn Glu Met Tyr Ser
145 150 155 160

Thr Tyr Phe Pro Arg Ala Asn Ala Ala Leu Gly Val Asn Asn Ile Asp
165 170 175

Pro Ala Trp Phe Glu Ser Thr Glu Tyr Tyr Lys Phe Ala Arg Thr Gly
180 185 190

Arg Lys Thr Ala Glu Arg Ser Gly Tyr Thr Thr Phe Xaa Pro Asn
195 200 205

Val Tyr Asp Phe Asn Tyr Met Lys Gln Glu Ala Ala Gly Gln Val Thr
210 215 220

Lys Ser Ala Leu Val Ser Glu Val Ile Tyr Gly Asn Asn Ala Gly Lys
225 230 235 240

Lys Ser Leu Asp Lys Thr Tyr Leu Ala Ala Ala Ser Ala Thr Gly Lys
245 250 255

Leu Thr Ile Ser Ala Leu His Val Val Thr Ser Val Ala Pro Ala Ala
260 265 270

Thr Gly Gly Tyr Gln Val Val Met Asn Gln Ile Asn Glu Gln Gly

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275 280 285

Asn Thr Val Gly Thr Lys Thr Val Thr Ala Asp Lys Val Phe Phe Ala
 290 295 300

Ala Gly Ser Ile Gly Thr Ser Lys Leu Leu Val Ala Met Lys Ala Gln
 305 310 315 320

Gly Gln Leu Ala Asn Leu Pro Gly Ala Val Gly Gln Glu Trp Gly His
 325 330 335

Asn Gly Asn Val Met Val Gly Arg Ala Asn His Met Trp Asp Ala Thr
 340 345 350

Gly Ala Lys Gln Ser Ala Ile Pro Val Met Gly Ile Asp Asn Trp Ala
 355 360 365

Asp Thr Ser Ala Pro Val Xaa Ala Glu Ile Ala Pro Phe Pro Ala Gly
 370 375 380

Thr Glu Leu Trp Val Ser Leu Tyr Leu Ala Ile Ala Lys Asn Pro Gln
 385 390 395 400

Arg Ala Gln Phe Gln Phe Asn Ser Ala Thr Gly Lys Val Gly Leu Asn
 405 410 415

Trp Gln Arg Ser Gln Asn Gln Pro Ser Ile Asp Met Ala Lys Lys Leu
 420 425 430

Phe Asp Lys Ile Asn Lys Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu
 435 440 445

Phe Gly Pro Thr Gln Thr Trp Gly Asp Gln Leu Thr Tyr His Pro Leu
 450 455 460

Gly Gly Cys Val Leu Gly Lys Ala Thr Asp Gly Tyr Gly Arg Leu Pro
 465 470 475 480

Glu Tyr Pro Gly Leu Tyr Val Met Asp Gly Ser Leu Val Pro Gly Asn
 485 490 495

Val Gly Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn
 500 505 510

Ile Glu Asn Ile Ile Ala Asn Asp Met Asn
 515 520

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<210> SEQ ID NO 36
<211> LENGTH: 523
<212> TYPE: PRT
<213> ORGANISM: Amycolatopsis mediterranei
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (142)..(142)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
  Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (211)..(211)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
  Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (377)..(377)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
  or Asp, provided that when Xaa142 is Met, then Xaa377 is not Phe

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<400> SEQUENCE: 36

Met Ala Ser Ala Ala Leu Ala Gly Arg Ala Thr Ala Ala Ser Ser Gln
 1 5 10 15

Pro Ala Val Ala Gly Ser Ala Ala Ile Ser Asp Gly Ala Arg Val
 20 25 30

Thr Ala Leu Val Ile Gly Thr Gly Tyr Gly Ser Val Ala Ala Leu
 35 40 45

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Arg Leu Ala Gln Ala Gly Val Asp Val Gln Met Val Glu Met Gly Met
 50 55 60

Ala Trp Asp Thr Pro Gly Ala Asp Gly Lys Ile Phe Cys Thr Thr Pro
 65 70 75 80

Asn Pro Asp Gln Arg Ser Phe Trp Leu Arg Thr Arg Thr Lys Gln Pro
 85 90 95

Leu Ser Asn Phe Leu Gly Phe Pro Ile Asp Lys Asp Ile Pro Arg Tyr
 100 105 110

Thr Gly Ile Leu Asp Ala Glu Glu Phe Ser Gly Ile Thr Val Tyr Gln
 115 120 125

Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val
 130 135 140

Thr Pro Lys Arg Glu Asn Phe Gly Ala Ile Leu Pro Thr Val Asp Ala
 145 150 155 160

Asn Glu Met Tyr Asp Val Tyr Tyr Pro Arg Ala Asn Ala Gly Leu Gly
 165 170 175

Val Ala Ser Val Arg Pro Ala Trp Phe Glu Thr Thr Asp Trp Tyr Gln
 180 185 190

Phe Ala Arg Val Gly Arg Lys Gln Ala Gln Arg Ser Gly Phe Pro Phe
 195 200 205

Val Phe Xaa Pro Asp Val Tyr Asp Trp Asp Tyr Met Glu Arg Glu Ala
 210 215 220

Ala Gly Thr Ala Thr Lys Ser Ala Leu Ala Gly Glu Ile Leu Phe Gly
 225 230 235 240

Asn Asn Tyr Gly Lys Ser Leu Gln Lys Thr Tyr Leu Pro Lys Ile
 245 250 255

Ala Ala Thr Gly Arg Val Thr Ile Ser Pro Leu His Arg Val Thr Gln
 260 265 270

Val Val Pro Ala Ser Gly Gly Tyr Thr Val Thr Ile Glu Gln Leu
 275 280 285

Thr Thr Asp Gly Ala Val Ser Ala Ile Lys Thr Val Thr Ala Ala Lys
 290 295 300

Val Phe Phe Ala Ala Gly Ser Val Gly Thr Ser Lys Leu Leu Val Lys
 305 310 315 320

Leu Lys Ala Thr Gly Ala Leu Pro Asn Leu Asn Gly Glu Val Gly Lys
 325 330 335

Gly Trp Gly Asp Asn Gly Asn Val Met Val Gly Arg Ala Asn Gln Ile
 340 345 350

Trp Asp Pro Thr Gly Ala Ser Gln Ser Thr Ile Pro Cys Gly Gly Ile
 355 360 365

Asp Asn Trp Ala Ala Gly Gly Ala Xaa Ala Glu Val Ala Pro Leu Pro
 370 375 380

Thr Gly Ile Glu Thr Trp Ala Ser Phe Tyr Leu Ser Ile Thr Lys Asn
 385 390 395 400

Pro Asn Arg Ala Gln Phe Thr Trp Asn Pro Thr Thr Arg Ala Val Asp
 405 410 415

Leu Asn Trp Gln Thr Ala Trp Lys Gln Pro Gly Ile Asp Met Ala Lys
 420 425 430

Thr Ile Phe Asp Lys Ile Asn Ala Thr Glu Gly Thr Ile Tyr Arg Thr
 435 440 445

Asp Leu Phe Gly Thr Tyr Lys Thr Trp Gly Asp His Leu Thr Tyr His
 450 455 460

Pro Leu Gly Gly Ala Val Leu Gly Lys Ala Thr Asp Asn Tyr Gly Arg

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465	470	475	480
Leu Ala Gly His Pro Gly Leu Tyr Ala Ile Asp Gly Ser Leu Ile Pro			
485	490	495	
Gly Asn Thr Ser Val Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu			
500	505	510	
Arg Asn Ile Glu Lys Ile Ile Ala Gln Asp Phe			
515	520		

<210> SEQ ID NO 37
<211> LENGTH: 547
<212> TYPE: PRT
<213> ORGANISM: Streptosporangium roseum
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (166)..(166)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (235)..(235)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (401)..(401)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa166 is Met, then Xaa401 is not Phe
<400> SEQUENCE: 37

Met Ser Asp Asn Thr Ser Gly Ser Thr Asp Ser Lys Gly Ile Ser Arg			
1	5	10	15

Arg Gly Phe Ile Ala Gly Thr Gly Ser Ile Leu Gly Val Ala Ala Leu			
20	25	30	

Thr Gly Arg Ala Thr Ala Ala Gln Ala Ala Ala Leu Pro Ala Ala Ala			
35	40	45	

Pro Ile Ser Ser Gly Ala His Val Pro Ala Leu Val Ile Gly Thr Gly			
50	55	60	

Tyr Gly Gly Ser Val Ala Ala Leu Arg Leu Ala Gln Ala Gly Val Asp			
65	70	75	80

Val His Met Ile Glu Met Gly Met Ala Trp Asp Thr Pro Gly Ser Asp			
85	90	95	

Gly Lys Ile Phe Cys Asn Thr Arg Glu Pro Asp Tyr Arg Ser Tyr Trp			
100	105	110	

Leu Arg Thr Lys Ser Lys Ala Pro Leu Asn Tyr Phe Leu Gly Phe Pro			
115	120	125	

Ile Asp Arg Asn Ile Pro Arg Tyr Thr Gly Ile Leu Asp Ala Glu Asp			
130	135	140	

Phe Ser Gly Ile Thr Val Tyr Gln Gly Arg Gly Val Gly Gly Ser			
145	150	155	160

Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Glu Asn Phe Gly			
165	170	175	

Ala Val Leu Pro Ser Val Asn Ala Ala Glu Met Tyr Asp Ile Tyr Tyr			
180	185	190	

Pro Arg Ala Asn Ala Gly Leu Gly Val Ser Ser Ile Asp Pro Ala Trp			
195	200	205	

Phe Asp Ser Thr Ala Cys Tyr Gln Tyr Ala Arg Val Gly Arg Lys His			
210	215	220	

Ala Gln Arg Ser Gly Phe Pro Phe Val Phe Xaa Pro Asp Val Tyr Asp			
225	230	235	240

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Trp Asp Tyr Met Lys Gln Glu Ala Ala Gly Thr Val Thr Lys Ser Ala
245 250 255

Leu Ala Gly Glu Ile Leu Tyr Gly Asn Asn His Gly Lys Lys Ser Leu
260 265 270

Gln Gln Thr Tyr Ile Ala Arg Ala Lys Ala Thr Gly Arg Val Ala Ile
275 280 285

Ser Pro Leu His Lys Val Thr Ser Val Ala Pro Ala Ala Gly Gly Gly
290 295 300

Tyr Thr Val Val Ile Asp Gln Ile Asn Thr Asn Gly Asp Thr Thr Ala
305 310 315 320

Thr Lys Thr Val Thr Ala Asp Arg Val Phe Phe Ala Ala Gly Ser Val
325 330 335

Gly Thr Ser Lys Leu Leu Val Lys Leu Lys Ala Thr Gly Ala Leu Pro
340 345 350

Asn Leu Asn Asp Glu Ile Gly Lys Gly Trp Gly Asp Asn Gly Asn Val
355 360 365

Met Cys Gly Arg Ala Asn His Met Trp Asp Pro Thr Gly Ser Leu Gln
370 375 380

Ser Ala Ile Pro Cys Ala Gly Ile Asp Asn Trp Ala Ala Gly Gly Ala
385 390 395 400

Xaa Ala Glu Val Ala Pro Leu Pro Thr Gly Ile Glu Thr Tyr Ala Ser
405 410 415

Phe Tyr Leu Ser Ile Thr Lys Asn Pro Asn Arg Ala Gln Phe Ser Trp
420 425 430

Asn Ala Ala Thr Gly Lys Val Asp Leu Asn Trp Gln Thr Ser Trp Lys
435 440 445

Gln Pro Ser Ile Asp Met Ala Lys Thr Ile Phe Asp Lys Ile Asn Ser
450 455 460

Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Thr Tyr Lys Ile
465 470 475 480

Trp Gly Asp His Leu Thr Tyr His Pro Leu Gly Gly Ala Val Leu Asn
485 490 495

Lys Ala Thr Asp Asn Tyr Gly Arg Leu Ala Gly His Pro Gly Leu Tyr
500 505 510

Val Ile Asp Gly Ser Leu Ile Pro Gly Asn Thr Ser Val Asn Pro Phe
515 520 525

Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Lys Ile Ile Ala
530 535 540

Thr Asp Leu
545

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<210> SEQ_ID NO 38
<211> LENGTH: 549
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp.
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (168)..(168)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (237)..(237)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (403)..(403)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
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or Asp, provided that when Xaa168 is Met, then Xaa403 is not Phe

<400> SEQUENCE: 38

Met	Ser	Asp	Lys	Ser	Leu	His	Ser	Lys	Val	Ser	Gly	Gly	Val	Ser	Arg
1															
														15	

Arg	Gly	Phe	Ile	Ala	Gly	Thr	Gly	Ser	Ile	Leu	Gly	Ala	Val	Ala	Leu
														30	

Thr	Val	Asn	Val	Thr	Pro	Ala	His	Ala	Glu	Pro	Ala	Thr	Thr	Thr	Ala
												35	40	45	

Ser	Gly	Pro	Ile	Glu	Ser	Gly	Ala	Arg	Val	Pro	Val	Leu	Val	Ile	Gly
												50	55	60	

Thr	Gly	Tyr	Gly	Gly	Ser	Val	Ala	Ala	Leu	Arg	Leu	Ala	Gln	Ala	Gly
												65	70	75	80

Val	Pro	Val	His	Met	Val	Glu	Met	Gly	Met	Ala	Trp	Asp	Thr	Pro	Gly
												85	90	95	

Ser	Asp	Gly	Lys	Ile	Phe	Ala	Asn	Thr	Thr	Lys	Pro	Asp	Tyr	Arg	Ser
												100	105	110	

Tyr	Trp	Leu	Arg	Thr	Arg	Thr	Lys	Ala	Pro	Leu	Ser	Asn	Phe	Leu	Gly
												115	120	125	

Phe	Pro	Ile	Asp	Lys	Asp	Val	Pro	Arg	Tyr	Thr	Gly	Ile	Leu	Asp	Ala
												130	135	140	

Glu	Glu	Met	Gly	Gly	Ile	Ile	Val	Tyr	Gln	Gly	Arg	Gly	Val	Gly	Gly
												145	150	155	160

Gly	Ser	Leu	Val	Asn	Gly	Gly	Xaa	Ala	Val	Thr	Pro	Lys	Arg	Gln	Asn
												165	170	175	

Phe	Ala	Ala	Ile	Leu	Pro	Ser	Val	Asp	Ala	Glu	Glu	Met	Tyr	Arg	Thr
												180	185	190	

Tyr	Tyr	Pro	Arg	Ala	Asn	Ala	Gly	Leu	Gly	Val	Gly	Leu	Ile	Asp	Pro
												195	200	205	

Val	Trp	Phe	Glu	Ala	Val	Asp	Cys	Tyr	Gln	Phe	Ala	Arg	Val	Gly	Arg
												210	215	220	

Lys	His	Ala	Gln	Arg	Ser	Gly	Phe	Pro	Phe	Val	Phe	Xaa	Pro	Asp	Val
												225	230	235	240

Tyr	Asp	Trp	Asp	Tyr	Met	Lys	Gln	Glu	Val	Ala	Gly	Thr	Val	Pro	Lys
												245	250	255	

Ser	Ala	Val	Asp	Gly	Glu	Ile	Leu	Tyr	Gly	Asn	Asn	Ala	Gly	Lys	Lys
												260	265	270	

Ser	Leu	Gln	Gln	Thr	Tyr	Leu	Ala	Ala	Arg	Ala	Thr	Gly	Lys	Val	
												275	280	285	

Thr	Ile	Ser	Pro	Leu	His	Arg	Val	Thr	Val	Ser	Pro	Ser	Asp	Gly	
												290	295	300	

Gly	Gly	Tyr	Thr	Val	Val	Met	Glu	Gln	Leu	Ser	Thr	Ser	Gly	Asp	Val
												305	310	315	320

Leu	Ala	Thr	Lys	Thr	Val	Thr	Ala	Gly	Arg	Val	Phe	Phe	Ala	Ala	Gly
												325	330	335	

Ser	Val	Gly	Thr	Ser	Lys	Leu	Leu	Val	Arg	Leu	Lys	Ala	Thr	Gly	Ala
												340	345	350	

Leu	Pro	Asn	Leu	Asn	Asp	Glu	Val	Gly	Lys	Gly	Trp	Gly	Asp	Asn	Gly
												355	360	365	

Asn	Val	Met	Cys	Gly	Arg	Ala	Asn	His	Met	Trp	Asp	Pro	Thr	Gly	Lys
												370	375	380	

Val	Gln	Ala	Ser	Ile	Pro	Cys	Gly	Gly	Ile	Asp	Asn	Trp	Asp	Ala	Gly
												385	390	395	400

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Gly Ala Xaa Ala Glu Val Ala Pro Leu Pro Thr Gly Ile Glu Thr Tyr
405 410 415

Ala Ser Phe Tyr Leu Ser Ile Thr Lys Asn Pro Asn Arg Ala Arg Phe
420 425 430

Ser Trp Asn Ala Ala Ala Gly Lys Val Glu Leu Asp Trp Gln Thr Ala
435 440 445

Trp Lys Gln Pro Ser Ile Asp Met Ala Lys Thr Ile Phe Asp Lys Ile
450 455 460

Asn Ala Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Thr Asn
465 470 475 480

Lys Val Trp Gly Asp His Leu Thr Tyr His Pro Leu Gly Ala Val
485 490 495

Leu Gly Lys Ala Thr Asp Asn Tyr Gly Arg Leu His Gly His Pro Gly
500 505 510

Leu Tyr Val Ile Asp Gly Ala Leu Ile Pro Gly Asn Thr Ser Val Asn
515 520 525

Pro Phe Ala Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Lys Ile
530 535 540

Ile Ala Thr Asp Leu
545

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<210> SEQ_ID NO 39
<211> LENGTH: 546
<212> TYPE: PRT
<213> ORGANISM: Catenulispora acidiphila
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (165)..(165)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (234)..(234)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (400)..(400)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa165 is Met, then Xaa400 is not Phe
```

<400> SEQUENCE: 39

Met Ser Ala Thr Ser Arg His Asp Pro Gly Ala Arg Gly Leu Ser Arg
1 5 10 15

Arg Gly Phe Leu Ala Gly Thr Gly Thr Val Leu Gly Ala Ala Ala Leu
20 25 30

Gly Gly Leu Ser Ala Ser Arg Ala Ser Ala Ala Gln Arg Ser Thr Pro
35 40 45

Ile Ser Asn Gly Ala His Val Gln Ala Leu Ile Ile Gly Thr Gly Tyr
50 55 60

Gly Gly Ser Val Ala Ala Leu Arg Leu Ala Gln Ala Gly Ile Ala Val
65 70 75 80

Glu Met Ile Glu Met Gly Met Ala Trp Asp Thr Pro Gly Ser Asp Gly
85 90 95

Lys Ile Phe Cys Asn Leu Thr Ser Pro Asp Gln Arg Ser Phe Trp Leu
100 105 110

Arg Thr Gln Thr Lys Gln Pro Val Gly Tyr Phe Leu Gly Ile Pro Ile
115 120 125

Asp Arg Ala Ile Pro Asn Tyr Thr Gly Ile Leu Asp Ala Glu Asp Phe
130 135 140

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Ala Gly Ile Thr Val Tyr Gln Gly Arg Gly Ile Gly Gly Ser Leu
 145 150 155 160
 Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Gln Glu Asn Phe Gly Ala
 165 170 175
 Ile Leu Pro Ser Val Asn Pro Ala Glu Met Tyr Asn Val Tyr Tyr Pro
 180 185 190
 Arg Ala Asn Ala Gly Leu Gly Ala Gly Val Val Pro Gln Ser Trp Phe
 195 200 205
 Thr Lys Thr Asp Trp Tyr Gln Phe Ala Arg Val Gly Gln Lys Gln Ala
 210 215 220
 Gly Arg Ser Gly Phe Pro Phe Gln Phe Xaa Pro Asp Val Tyr Asp Trp
 225 230 235 240
 Asn Tyr Met Gln Gln Glu Asp Ala Gly Thr Val Pro Lys Ser Ala Leu
 245 250 255
 Gly Gln Glu Leu Leu Tyr Gly Asn Asn Tyr Gly Lys Lys Ser Leu Gln
 260 265 270
 Lys Thr Tyr Ile Pro Ala Ala Leu Ala Thr Gly Lys Val Asn Ile Ser
 275 280 285
 Pro Leu His Lys Val Thr Ser Val Ser Pro Ala Ser Gly Gly Tyr
 290 295 300
 Thr Val Leu Met Asn Gln Leu Asp Thr Ser Gly Asn Val Val Val Thr
 305 310 315 320
 Lys Glu Val Thr Ala Asp Lys Val Val Phe Ala Ala Gly Ser Val Gly
 325 330 335
 Thr Ser Lys Leu Leu Val Gln Met Arg Asp Thr Gly Gln Leu Pro His
 340 345 350
 Leu Asn Asp Gln Val Gly Gln Gly Trp Gly Asp Asn Gly Asn Ile Met
 355 360 365
 Val Gly Arg Ala Asn Gln Ile Trp Asp Pro Thr Gly Ser Lys Gln Ser
 370 375 380
 Thr Val Pro Cys Gly Gly Ile Asp Asn Trp Thr Lys Gly Ala Xaa
 385 390 395 400
 Ala Glu Val Ala Pro Leu Pro Ile Gly Ile Glu Thr Trp Ala Ser Leu
 405 410 415
 Tyr Leu Ser Ile Thr Lys Asn Pro His Arg Ala Gln Phe Thr Trp Asn
 420 425 430
 Ala Ala Thr Gln Lys Val Asp Leu Ser Trp Gln Leu Ala Trp Lys Gln
 435 440 445
 Asp Gly Ile Thr Met Ala Lys Ser Ile Phe Asp Lys Ile Asn Ser Thr
 450 455 460
 Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Ser Tyr Lys Thr Trp
 465 470 475 480
 Gln Asp Gln Leu Thr Tyr His Pro Leu Gly Gly Ala Val Leu Asn Gln
 485 490 495
 Ala Thr Asp Asn Tyr Gly Arg Leu Thr Ala Tyr Pro Gly Leu Tyr Val
 500 505 510
 Met Asp Gly Ala Leu Ile Pro Gly Asn Thr Ser Val Asn Pro Phe Val
 515 520 525
 Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Asn Ile Ile Ala Asn
 530 535 540
 Gly Gly
 545

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<210> SEQ ID NO 40
<211> LENGTH: 550
<212> TYPE: PRT
<213> ORGANISM: Streptomyces roseosporus
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (169)..(169)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (238)..(238)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (404)..(404)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa169 is Met, then Xaa404 is not Phe

<400> SEQUENCE: 40

Met Cys His Met Asn Asp Thr Ser Met Gln Asn Ser Glu Thr Lys Gly
1 5 10 15

Val Ser Arg Arg Phe Ile Thr Gly Thr Gly Ser Leu Leu Gly Ala
20 25 30

Ala Ala Ile Ala Gly His Ala Pro Arg Ala Trp Ala Asp Val Arg Ala
35 40 45

Val Ala Ala Pro Ile Gly Ser Gly Ala His Val Pro Val Leu Val Val
50 55 60

Gly Thr Gly Tyr Gly Gly Ser Val Ala Ala Leu Arg Leu Ala Glu Ala
65 70 75 80

Gly Thr Asp Val His Met Val Glu Met Ala Trp Asp Thr Pro
85 90 95

Gly Ala Asp Gly Lys Ile Phe Ala Asn Thr Thr Arg Pro Asp Asp Arg
100 105 110

Ser Phe Trp Leu Arg Thr Arg Thr Lys Gln Pro Leu Ser Asn Phe Leu
115 120 125

Gly Phe Pro Leu Asp Lys Asp Val Asn Arg Tyr Thr Gly Ile Leu Asp
130 135 140

Ala Glu Glu Phe Gly Gly Ile Thr Val Tyr Gln Gly Arg Gly Val Gly
145 150 155 160

Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Arg Arg Glu
165 170 175

Asn Phe Gly Ala Ile Leu Pro Thr Val Asn Ala Ala Glu Met Tyr Ser
180 185 190

Thr Tyr Tyr Pro Arg Ala Asn Ser Gly Leu Gly Val Thr Thr Ile Asp
195 200 205

Pro Ala Trp Phe Asp Ser Val Asp Cys Tyr Gln Tyr Ala Arg Val Gly
210 215 220

Arg Lys His Ala Gln Arg Ser Gly Phe Pro Phe Leu Phe Xaa Pro Ala
225 230 235 240

Val Tyr Asp Trp Asp Tyr Met Lys Gln Glu Ala Ala Gly Thr Val Pro
245 250 255

Lys Ser Ala Leu Asp Gly Glu Ile Leu Tyr Gly Asn Asn His Gly Lys
260 265 270

Lys Ser Leu Gln Lys Thr Tyr Ile Asp Arg Ile Arg Ala Thr Gly Arg
275 280 285

Val Thr Ile Ser Pro Leu His Lys Val Thr Thr Val Thr Pro Ala Pro
290 295 300

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Gly Gly Gly Tyr Thr Val Leu Ile Asp Gln Leu Asp Thr Gly Gly Arg
305 310 315 320

Thr Thr Ala Thr Lys Thr Val Thr Ala Asp Lys Val Phe Phe Ala Ala
325 330 335

Gly Ser Val Gly Thr Ser Lys Leu Leu Val Gly Leu Lys Ala Thr Gly
340 345 350

Ala Leu Pro Leu Leu Asn Asp Glu Ile Gly Arg Gly Trp Gly Asp Asn
355 360 365

Gly Asn Val Met Cys Gly Arg Ala Asn His Leu Trp Asp Pro Thr Gly
370 375 380

Lys Val Gln Ser Ser Ile Pro Thr Gly Gly Ile Asp Asn Trp Asp Ala
385 390 395 400

Gly Gly Ala Xaa Ala Glu Ile Ala Pro Leu Pro Thr Gly Ile Glu Thr
405 410 415

Trp Ala Ser Phe Tyr Leu Ser Ile Thr Lys Asn Pro His Arg Ala Arg
420 425 430

Phe Thr Trp Asn Ala Ala Gly Lys Ala Glu Leu Asp Trp Arg Thr
435 440 445

Ala Trp Lys Gln Pro Ser Ile Asp Ala Ala Lys Thr Ile Phe Asp Lys
450 455 460

Ile Asn Gln Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Val
465 470 475 480

Tyr Lys Ile Trp Gly Asp His Leu Thr Tyr His Pro Leu Gly Ala
485 490 495

Val Leu Asp Lys Ala Thr Asp Asn Tyr Gly Arg Leu His Gly Tyr Ser
500 505 510

Gly Leu Tyr Val Ile Asp Gly Ala Leu Ile Pro Gly Asn Thr Ser Val
515 520 525

Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg
530 535 540

Ile Ile Ala Thr Asp Leu
545 550

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<210> SEQ_ID NO 41
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Streptomyces roseosporus
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (121)..(121)
<223> OTHER_INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (190)..(190)
<223> OTHER_INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (356)..(356)
<223> OTHER_INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa121 is Met, then Xaa356 is not Phe

<400> SEQUENCE: 41

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Met Ala Ala Pro Ile Gly Ser Gly Ala His Val Pro Val Leu Val Val
1 5 10 15

Gly Thr Gly Tyr Gly Gly Ser Val Ala Ala Leu Arg Leu Ala Glu Ala
20 25 30

Gly Thr Asp Val His Met Val Glu Met Gly Met Ala Trp Asp Thr Pro

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160

35	40	45
Gly Ala Asp Gly Lys Ile Phe Ala Asn Thr Thr Arg Pro Asp Asp Arg		
50	55	60
Ser Phe Trp Leu Arg Thr Arg Thr Lys Gln Pro Leu Ser Asn Phe Leu		
65	70	75
Gly Phe Pro Leu Asp Lys Asp Val Asn Arg Tyr Thr Gly Ile Leu Asp		
85	90	95
Ala Glu Glu Phe Gly Gly Ile Thr Val Tyr Gln Gly Arg Gly Val Gly		
100	105	110
Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Arg Arg Glu		
115	120	125
Asn Phe Gly Ala Ile Leu Pro Thr Val Asn Ala Ala Glu Met Tyr Ser		
130	135	140
Thr Tyr Tyr Pro Arg Ala Asn Ser Gly Leu Gly Val Thr Thr Ile Asp		
145	150	155
Pro Ala Trp Phe Asp Ser Val Asp Cys Tyr Gln Tyr Ala Arg Val Gly		
165	170	175
Arg Lys His Ala Gln Arg Ser Gly Phe Pro Phe Leu Phe Xaa Pro Ala		
180	185	190
Val Tyr Asp Trp Asp Tyr Met Lys Gln Glu Ala Ala Gly Thr Val Pro		
195	200	205
Lys Ser Ala Leu Asp Gly Glu Ile Leu Tyr Gly Asn Asn His Gly Lys		
210	215	220
Lys Ser Leu Gln Lys Thr Tyr Ile Asp Arg Ile Arg Ala Thr Gly Arg		
225	230	235
Val Thr Ile Ser Pro Leu His Lys Val Thr Thr Val Thr Pro Ala Pro		
245	250	255
Gly Gly Gly Tyr Thr Val Leu Ile Asp Gln Leu Asp Thr Gly Gly Arg		
260	265	270
Thr Thr Ala Thr Lys Thr Val Thr Ala Asp Lys Val Phe Phe Ala Ala		
275	280	285
Gly Ser Val Gly Thr Ser Lys Leu Leu Val Gly Leu Lys Ala Thr Gly		
290	295	300
Ala Leu Pro Leu Leu Asn Asp Glu Ile Gly Arg Gly Trp Gly Asp Asn		
305	310	315
Gly Asn Val Met Cys Gly Arg Ala Asn His Leu Trp Asp Pro Thr Gly		
325	330	335
Lys Val Gln Ser Ser Ile Pro Thr Gly Gly Ile Asp Asn Trp Asp Ala		
340	345	350
Gly Gly Ala Xaa Ala Glu Ile Ala Pro Leu Pro Thr Gly Ile Glu Thr		
355	360	365
Trp Ala Ser Phe Tyr Leu Ser Ile Thr Lys Asn Pro His Arg Ala Arg		
370	375	380
Phe Thr Trp Asn Ala Ala Ala Gly Lys Ala Glu Leu Asp Trp Arg Thr		
385	390	395
Ala Trp Lys Gln Pro Ser Ile Asp Ala Ala Lys Thr Ile Phe Asp Lys		
405	410	415
Ile Asn Gln Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Val		
420	425	430
Tyr Lys Ile Trp Gly Asp His Leu Thr Tyr His Pro Leu Gly Gly Ala		
435	440	445
Val Leu Asp Lys Ala Thr Asp Asn Tyr Gly Arg Leu His Gly Tyr Ser		
450	455	460

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Gly Leu Tyr Val Ile Asp Gly Ala Leu Ile Pro Gly Asn Thr Ser Val
 465 470 475 480

Asn Pro Phe Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg
 485 490 495

Ile Ile Ala Thr Asp Leu
 500

<210> SEQ ID NO 42
 <211> LENGTH: 547
 <212> TYPE: PRT
 <213> ORGANISM: Streptomyces sp.
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (166)..(166)
 <223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
 Tyr, Lys or Ser
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (235)..(235)
 <223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (401)..(401)
 <223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa166 is Met, then Xaa401 is not Phe

<400> SEQUENCE: 42

Met Gly Asp Thr Thr Val His Lys Gly Gly Thr Gln Gly Val Ser Arg
 1 5 10 15

Arg Arg Phe Ile Thr Gly Thr Gly Ser Leu Leu Gly Gly Ala Ala Ile
 20 25 30

Ala Gly His Thr Ala Pro Ala Trp Ala Thr Val Arg Ala Ala Ala Ala
 35 40 45

Pro Ile Gly Ser Gly Ala Arg Val Pro Ala Leu Val Ile Gly Thr Gly
 50 55 60

Tyr Gly Gly Ser Val Ala Ala Leu Arg Leu Ala Gln Ala Gly Thr Asp
 65 70 75 80

Val His Met Val Glu Met Gly Met Ala Trp Asp Thr Pro Gly Ala Asp
 85 90 95

Gly Lys Ile Phe Ala Asn Thr Thr Arg Pro Asp Asp Arg Ser Phe Trp
 100 105 110

Leu Arg Thr Arg Thr Lys Gln Pro Leu Ser Asn Phe Leu Gly Phe Pro
 115 120 125

Ile Asp Arg Ser Val Asn Arg Tyr Thr Gly Ile Leu Asp Ala Glu Glu
 130 135 140

Phe Ala Gly Ile Thr Val Tyr Gln Gly Arg Gly Val Gly Gly Ser
 145 150 155 160

Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Arg Arg Glu Asn Phe Gly
 165 170 175

Ala Ile Leu Pro Thr Val Asn Ala Gln Glu Met Tyr Ser Thr Tyr Tyr
 180 185 190

Pro Arg Ala Asn Ser Gly Leu Gly Val Thr Thr Ile Asp Pro Ala Trp
 195 200 205

Phe Asp Ser Val Asp Cys Tyr Gln Tyr Ala Arg Val Gly Arg Lys His
 210 215 220

Ala Gln Arg Ser Gly Phe Pro Phe Leu Phe Xaa Pro Ala Val Tyr Asp
 225 230 235 240

Trp Asp Tyr Met Lys Gln Glu Ala Ala Gly Thr Val Pro Arg Ser Ala

-continued

245	250	255
Leu Asp Ala Glu Ile Leu Tyr Gly Asn Asn Tyr Gly Lys Lys Ser Leu		
260	265	270
Gln Lys Thr Tyr Ile Asp Arg Ile Arg Ala Thr Gly Arg Val Thr Ile		
275	280	285
Ser Pro Leu His Arg Val Thr Arg Val Thr Pro Ala Pro Gly Gly Gly		
290	295	300
Tyr Thr Val Leu Ile Asp Gln Leu Asn Thr Ala Gly Gln Thr Thr Ala		
305	310	315
320		
Thr Lys Thr Val Thr Ala Asp Lys Val Phe Phe Ala Ala Gly Ser Val		
325	330	335
Gly Thr Ser Lys Leu Leu Val Gly Leu Lys Ala Thr Gly Ala Leu Pro		
340	345	350
Leu Leu Asn Asp Glu Ile Gly Lys Gly Trp Gly Asp Asn Gly Asn Val		
355	360	365
Met Cys Gly Arg Ala Asn His Leu Trp Asp Pro Thr Gly Lys Val Gln		
370	375	380
Ser Ser Ile Pro Thr Gly Gly Ile Asp Asn Trp Asp Ala Gly Gly Ala		
385	390	395
400		
Xaa Ala Glu Val Ala Pro Leu Pro Thr Gly Ile Glu Thr Trp Ala Ser		
405	410	415
Phe Tyr Leu Ser Ile Thr Lys Asn Pro His Arg Ala Arg Phe Thr Trp		
420	425	430
Asn Ala Ala Ala Gly Lys Ala Glu Leu Asp Trp Gln Thr Ala Trp Lys		
435	440	445
Gln Pro Ser Ile Asp Ala Ala Lys Thr Ile Phe Asp Lys Ile Asn Gln		
450	455	460
Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Val His Lys Ile		
465	470	475
480		
Trp Gly Asp His Leu Thr Tyr His Pro Leu Gly Gly Ala Val Leu Asp		
485	490	495
Lys Ala Thr Asp Asn Tyr Gly Arg Leu His Gly Tyr Thr Gly Leu Tyr		
500	505	510
Val Ile Asp Gly Ala Leu Ile Pro Gly Asn Thr Ser Val Asn Pro Phe		
515	520	525
Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg Ile Ile Ala		
530	535	540
Thr Asp Leu		
545		

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<210> SEQ_ID NO 43
<211> LENGTH: 547
<212> TYPE: PRT
<213> ORGANISM: Streptomyces griseus
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (166)..(166)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (235)..(235)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (401)..(401)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa166 is Met, then Xaa401 is not Phe

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<400> SEQUENCE: 43

Met	Gly	Asp	Thr	Thr	Val	His	Lys	Gly	Gly	Thr	Gln	Gly	Val	Ser	Arg
1															
														15	

Arg	Arg	Phe	Ile	Thr	Gly	Thr	Gly	Ser	Leu	Leu	Gly	Ala	Ala	Ile		
														20	25	30

Ala	Gly	His	Thr	Ala	Pro	Ala	Trp	Ala	Thr	Val	Arg	Ala	Ala	Ala		
														35	40	45

Pro	Ile	Gly	Ser	Gly	Ala	Arg	Val	Pro	Ala	Leu	Val	Ile	Gly	Thr	Gly	
														50	55	60

Tyr	Gly	Gly	Ser	Val	Ala	Ala	Leu	Arg	Leu	Ala	Gln	Ala	Gly	Thr	Asp			
															65	70	75	80

Val	His	Met	Val	Glu	Met	Gly	Met	Ala	Trp	Asp	Thr	Pro	Gly	Ala	Asp	
														85	90	95

Gly	Lys	Ile	Phe	Ala	Asn	Thr	Thr	Arg	Pro	Asp	Asp	Arg	Ser	Phe	Trp	
														100	105	110

Leu	Arg	Thr	Arg	Thr	Lys	Gln	Pro	Leu	Ser	Asn	Phe	Leu	Gly	Phe	Pro	
														115	120	125

Ile	Asp	Arg	Ser	Val	Asn	Arg	Tyr	Thr	Gly	Ile	Leu	Asp	Ala	Glu	Glu	
														130	135	140

Phe	Ala	Gly	Ile	Thr	Val	Tyr	Gln	Gly	Arg	Gly	Val	Gly	Gly	Ser			
														145	150	155	160

Leu	Val	Asn	Gly	Gly	Xaa	Ala	Val	Thr	Pro	Arg	Arg	Glu	Asn	Phe	Gly	
														165	170	175

Ala	Ile	Leu	Pro	Thr	Val	Asn	Ala	Gln	Glu	Met	Tyr	Ser	Thr	Tyr	Tyr	
														180	185	190

Pro	Arg	Ala	Asn	Ser	Gly	Leu	Gly	Val	Thr	Ile	Asp	Pro	Ala	Trp		
														195	200	205

Phe	Asp	Ser	Val	Asp	Cys	Tyr	Gln	Tyr	Ala	Arg	Val	Gly	Arg	Lys	His	
														210	215	220

Ala	Gln	Arg	Ser	Gly	Phe	Pro	Phe	Leu	Phe	Xaa	Pro	Ala	Val	Tyr	Asp		
														225	230	235	240

Trp	Asp	Tyr	Met	Lys	Gln	Glu	Ala	Ala	Gly	Thr	Val	Pro	Arg	Ser	Ala	
														245	250	255

Leu	Asp	Ala	Glu	Ile	Leu	Tyr	Gly	Asn	Asn	Tyr	Gly	Lys	Ser	Leu		
														260	265	270

Gln	Lys	Thr	Tyr	Ile	Asp	Arg	Ile	Arg	Ala	Thr	Gly	Arg	Val	Thr	Ile	
														275	280	285

Ser	Pro	Leu	His	Lys	Val	Thr	Arg	Val	Thr	Pro	Ala	Pro	Gly	Gly		
														290	295	300

Tyr	Thr	Val	Leu	Ile	Asp	Gln	Leu	Asn	Thr	Ala	Gly	Gln	Thr	Thr	Ala		
														305	310	315	320

Thr	Lys	Thr	Val	Thr	Ala	Asp	Lys	Val	Phe	Phe	Ala	Ala	Gly	Ser	Val	
														325	330	335

Gly	Thr	Ser	Lys	Leu	Leu	Val	Gly	Leu	Lys	Ala	Thr	Gly	Ala	Leu	Pro	
														340	345	350

Leu	Leu	Asn	Asp	Glu	Ile	Gly	Lys	Gly	Trp	Gly	Asp	Asn	Gly	Asn	Val	
														355	360	365

Met	Cys	Gly	Arg	Ala	Asn	His	Leu	Trp	Asp	Pro	Thr	Gly	Lys	Val	Gln	
														370	375	380

Ser	Ser	Ile	Pro	Thr	Gly	Gly	Ile	Asp	Asn	Trp	Asp	Ala	Gly	Ala			
														385	390	395	400

Xaa Ala Glu Val Ala Pro Leu Pro Thr Gly Ile Glu Thr Trp Ala Ser

-continued

405	410	415
Phe Tyr Leu Ser Ile Thr Lys Asn Pro His Arg Ala Arg Phe Thr Trp		
420	425	430
Asn Ala Ala Ala Gly Lys Ala Glu Leu Asp Trp Gln Thr Ala Trp Lys		
435	440	445
Gln Pro Ser Ile Asp Ala Ala Lys Thr Ile Phe Asp Lys Ile Asn Gln		
450	455	460
Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Val His Lys Ile		
465	470	475
Trp Gly Asp His Leu Thr Tyr His Pro Leu Gly Gly Ala Val Leu Asp		
485	490	495
Lys Ala Thr Asp Asn Tyr Gly Arg Leu His Gly Tyr Thr Gly Leu Tyr		
500	505	510
Val Ile Asp Gly Ala Leu Ile Pro Gly Asn Thr Ser Val Asn Pro Phe		
515	520	525
Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Arg Ile Ile Ala		
530	535	540
Thr Asp Leu		
545		

<210> SEQ ID NO 44
<211> LENGTH: 546
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp.
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (165)..(165)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln, Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (234)..(234)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser, Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (400)..(400)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His or Asp, provided that when Xaa165 is Met, then Xaa400 is not Phe

<400> SEQUENCE: 44		
Met Pro Asp Lys Gly Ser Lys Gly Phe Ser Arg Arg Gly Phe Ile Ala		
1	5	10
Arg Thr Ser Ser Ile Leu Gly Ala Val Ala Val Ala Gly Gly Ala Ala		
20	25	30
Ala Thr Thr Ala Arg Ala Ala Val Ala Thr Ser Ala Thr Ala Ala Pro		
35	40	45
Ile Asp Ser Gly Ala His Val Pro Val Leu Ile Ile Gly Thr Gly Tyr		
50	55	60
Gly Gly Ser Val Ala Ala Leu Arg Leu Ala Gln Ala Gly Val Asp Val		
65	70	75
His Met Ile Glu Met Gly Met Ala Trp Asp Thr Pro Gly Ser Asp Gly		
85	90	95
Lys Ile Phe Ala Asn Thr Thr Arg Pro Asp Tyr Arg Ser Phe Trp Leu		
100	105	110
Arg Thr Arg Thr Lys Ala Pro Ile Ser Asn Phe Leu Gly Phe Pro Ile		
115	120	125
Asp Lys Asp Val Ala Arg Tyr Thr Gly Ile Leu Asp Ala Glu Glu Phe		
130	135	140

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Asn Gly Ile Thr Val Tyr Gln Gly Arg Gly Val Gly Gly Ser Leu
 145 150 155 160
 Val Asn Gly Gly Xaa Ala Val Thr Pro Lys Arg Glu Arg Phe Gly Ala
 165 170 175
 Val Leu Pro Ser Val Asp Ala Asp Glu Met Tyr Asp Val Tyr Tyr Pro
 180 185 190
 Arg Ala Asn Ala Gly Leu Gly Val Thr Asn Val Asp Gln Ala Trp Trp
 195 200 205
 Glu Thr Ala Pro Cys Tyr Gln Tyr Ala Arg Val Gly Arg Lys His Ala
 210 215 220
 Gln Arg Ser Gly Phe Pro Phe Val Phe Xaa Pro Asn Val Tyr Asp Trp
 225 230 235 240
 Glu Tyr Met Lys Gln Glu Ala Gly Thr Val Pro Arg Ser Ser Leu
 245 250 255
 Asp Gly Glu Val Leu Tyr Gly Asn Asn Tyr Gly Lys Lys Ser Val Gln
 260 265 270
 Lys Thr Tyr Ile Ala Gln Ala Lys Ala Thr Gly Arg Val Ser Ile Ser
 275 280 285
 Pro Gln His Lys Val Thr Ser Val Ala Pro Ala Thr Gly Gly Tyr
 290 295 300
 Thr Val Ser Ile Asp Gln Ile Asn Thr Thr Gly Asp Thr Thr Ala Thr
 305 310 315 320
 Lys Thr Val Thr Ala Asp Arg Val Phe Phe Ala Ala Gly Ser Val Gly
 325 330 335
 Thr Ser Lys Leu Leu Val Arg Leu Lys Ala Thr Gly Arg Leu Pro Leu
 340 345 350
 Leu Asn Asp Glu Val Gly Lys Gly Trp Gly Asp Asn Gly Asn Val Met
 355 360 365
 Cys Gly Arg Ala Asn His Ile Trp Asp Ala Thr Gly Lys Leu Gln Ala
 370 375 380
 Ser Met Pro Thr Ala Gly Ile Asp Asn Trp Asp Ala Gly Gly Ala Xaa
 385 390 395 400
 Ala Glu Val Ala Pro Leu Pro Thr Gly Ile Glu Thr Tyr Ala Ser Leu
 405 410 415
 Tyr Leu Ser Ile Thr Lys Asn Pro His Arg Ala Glu Phe Ser Trp Asn
 420 425 430
 Ala Ala Thr Gly Asn Val Asp Leu Asn Trp Gln Arg Ala Trp Lys Gln
 435 440 445
 Pro Ala Ile Asp Met Ala Lys Ser Ile Phe Asp Lys Ile Asn Ser Lys
 450 455 460
 Glu Gly Thr Ile Tyr Arg Ser Asp Leu Phe Gly Gly Asn Lys Val Trp
 465 470 475 480
 Gly Asp His Leu Thr Tyr His Pro Leu Gly Gly Ala Val Leu Asp Lys
 485 490 495
 Ala Thr Asp Asn Tyr Gly Arg Leu His Gly Tyr Ser Gly Leu Tyr Val
 500 505 510
 Ile Asp Gly Ser Leu Ile Pro Gly Asn Thr Ser Val Asn Pro Phe Val
 515 520 525
 Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Lys Ile Ile Ala Thr
 530 535 540
 Asp Leu
 545

-continued

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<210> SEQ_ID NO 45
<211> LENGTH: 547
<212> TYPE: PRT
<213> ORGANISM: Streptomyces pristinaespiralis
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (166)..(166)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
    Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (235)..(235)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
    Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (401)..(401)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
    or Asp, provided that when Xaa166 is Met, then Xaa401 is not Phe

<400> SEQUENCE: 45

```

Met Asn Ala Ala Pro Leu Pro Arg Pro Ser Gly Arg Asp Pro Ser Arg
 1 5 10 15

Arg Gln Leu Leu Ala Gly Thr Gly Ser Ile Leu Gly Ala Val Ile Leu
 20 25 30

Ala Gly His Gly Pro Ala Ala Ala Arg Ala Lys Ala Ala Pro Ala Ala
 35 40 45

Ala Ile Pro Asp Gly Ala His Val Pro Ala Leu Val Ile Gly Thr Gly
 50 55 60

Tyr Gly Gly Ser Val Ala Ala Leu Arg Leu Ala Arg Ala Gly Val Asp
 65 70 75 80

Val His Met Ile Glu Met Gly Met Ser Trp Asp Thr Pro Gly Pro Asp
 85 90 95

Gly Lys Val Phe Ala Asn Thr Thr Arg Pro Asp His Arg Ser Phe Trp
 100 105 110

Leu Arg Thr Arg Thr Lys Gln Pro Leu Ser Asp Phe Leu Gly Phe Pro
 115 120 125

Leu Asp Lys Asp Val Pro Arg Tyr Thr Gly Ile Leu Asp Ala Glu Glu
 130 135 140

Phe Gly Gly Ile Thr Val Tyr Gln Gly Arg Gly Val Gly Gly Ser
 145 150 155 160

Leu Val Asn Gly Gly Xaa Ala Val Thr Pro Arg Arg Glu Asn Phe Gly
 165 170 175

Ala Val Leu Pro Ser Val Asn Ala Asp Glu Met Tyr Gly Ile Tyr Tyr
 180 185 190

Pro Arg Ala Asn Ala Ala Leu Gly Val Gly Val Val Asp Gln Gly Trp
 195 200 205

Trp Glu Ser Ala Ala Cys Tyr Gln Tyr Ala Arg Val Gly Arg Lys His
 210 215 220

Ala Glu Arg Ser Gly Phe Pro Phe Val Leu Xaa Pro Gly Val Tyr Asp
 225 230 235 240

Trp Asp Tyr Leu Glu Gln Glu Ala Ala Gly Thr Val Pro Ala Ser Ala
 245 250 255

Leu Glu Gly Glu Val Leu Phe Gly Asn Asn His Gly Lys Lys Ser Leu
 260 265 270

Pro Lys Thr Tyr Leu Ala Arg Ala Ala Ala Thr Gly Arg Val Val Ile
 275 280 285

Ser Pro Leu His Lys Val Thr Ser Val Ala Pro Ala Gly Gly Gly
 290 295 300

-continued

Tyr Thr Val Val Met Glu Gln Leu Asn Thr Gly Gly Asp Val Thr Ala
305 310 315 320

Val Lys Ala Val Thr Ala Asp Arg Val Phe Phe Ala Ala Gly Ser Val
325 330 335

Gly Thr Ser Lys Leu Leu Thr Arg Leu Lys Ala Thr Gly Val Leu Pro
340 345 350

Gly Leu Asn Gly Glu Ile Gly Lys Gly Trp Gly Asp Asn Gly Asn Val
355 360 365

Met Cys Gly Arg Ala Asn His Met Trp Asp Ala Thr Gly Arg Leu Gln
370 375 380

Ala Ser Met Pro Thr Ala Gly Ile Asp Asn Trp Gln Ala Gly Gly Ala
385 390 395 400

Xaa Ala Glu Val Ala Pro Leu Pro Thr Gly Ile Glu Thr Tyr Ala Ser
405 410 415

Phe Tyr Leu Ser Ile Thr Arg Asn Pro His Arg Ala Ala Phe Ser Trp
420 425 430

Asp Ala Ala Ala Gly Lys Val Val Leu Asp Trp Arg Thr Ala Trp Lys
435 440 445

Gln Pro Ser Ile Asp Ala Ala Arg Thr Ile Phe Asp Arg Ile Asn Ala
450 455 460

Lys Glu Gly Thr Ile Tyr Arg Thr Asp Leu Phe Gly Ala Tyr Lys Ile
465 470 475 480

Trp Gly Asp His Leu Thr Tyr His Pro Leu Gly Gly Ala Val Leu Asn
485 490 495

Arg Ala Thr Asp Asn Tyr Gly Arg Leu His Gly His Pro Gly Leu Tyr
500 505 510

Val Ile Asp Gly Ser Leu Ile Pro Gly Asn Thr Ser Val Asn Pro Phe
515 520 525

Val Thr Ile Thr Ala Leu Ala Glu Arg Asn Ile Glu Lys Ile Ile Ala
530 535 540

Thr Asp Leu
545

<210> SEQ ID NO 46
<211> LENGTH: 543
<212> TYPE: PRT
<213> ORGANISM: Actinosynnema mirum
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (163)..(163)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (232)..(232)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (397)..(397)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
or Asp, provided that when Xaa163 is Met, then Xaa397 is not Phe

<400> SEQUENCE: 46

Met Thr Arg Ser Val Ser Arg Arg Ser Phe Leu Ala Gly Ala Gly Thr
1 5 10 15

Ala Leu Gly Ala Thr Ala Phe Ser Gly Gly Ala Ser Ala Ser Gly Ser
20 25 30

Thr Ala Pro Gly Ala Pro Ala Ser Gly Arg Ser Pro Ala Gly Ile Pro
35 40 45

-continued

Asp Gly Ala Arg Val Pro Ala Leu Val Val Gly Ser Gly Tyr Gly Gly
50 55 60

Ala Val Ala Ala Leu Arg Leu Ala Gln Ala Gly Val Pro Val His Val
65 70 75 80

Val Glu Lys Gly Arg Ser Trp Asp Glu Pro Gly Trp Asp Gly Lys Val
85 90 95

Phe Ala Asn Met Leu Asn Pro Asp Glu Arg Ser Tyr Trp Leu Arg Thr
100 105 110

Trp Thr Lys Gln Pro Leu Ser Asn Phe Leu Gly Leu Pro Val Asp Arg
115 120 125

Ala Val Pro Arg Arg Thr Gly Ile Leu Asp Ala Glu Glu Phe Ala Gly
130 135 140

Ile Thr Val Tyr Gln Gly Arg Gly Val Gly Gly Ser Leu Val Asn
145 150 155 160

Gly Gly Xaa Ala Val Thr Pro Arg Arg Glu Arg Phe Ala Ala Val Leu
165 170 175

Pro Gly Val Asp Pro Glu Glu Met Tyr Ser Thr Tyr Tyr Pro Leu Ala
180 185 190

Asn Ala Glu Leu Gly Thr Gly Leu Val Asp Pro Asp Trp Trp Glu Gln
195 200 205

Ala Glu Cys Tyr Arg Tyr Ala Arg Val Gly Arg Ala Gln Ala Gln Arg
210 215 220

Ser Gly Phe Pro Phe Glu Leu Xaa Pro Gly Val Tyr Asp Trp Ala His
225 230 235 240

Leu Glu Arg Glu Ala Gly Thr Ala Pro Arg Ser Ala Leu Ala Ala
245 250 255

Glu Val Ile Tyr Gly Asn Asn His Gly Lys Leu Ser Leu Pro Arg Thr
260 265 270

Tyr Leu Ala Arg Ala Leu Ala Thr Gly Arg Val Thr Ile Ser Ala Leu
275 280 285

His Glu Val Thr Ser Val Arg Ala Val Gly Gly Tyr Glu Ala Leu
290 295 300

Leu Asp Val Leu Asp Thr Asn Gly Arg Val Thr Ser Thr Lys Arg Val
305 310 315 320

Glu Ala Glu Arg Val Phe Phe Ala Ala Gly Ser Val Gly Thr Ser Lys
325 330 335

Leu Leu Thr Arg Leu Arg Asp Thr Gly Ala Leu Pro Ala Leu Ser Pro
340 345 350

Glu Val Gly Leu Gly Trp Gly Glu Asn Gly Asn Val Met Val Gly Arg
355 360 365

Ala Asn Lys Ala Ser Asp Pro Thr Gly Ala Leu Gln Ser Cys Ile Pro
370 375 380

Thr Gly Gly Ile Asp Asn Trp Ala Ala Gly Gly Ala Xaa Ala Glu Val
385 390 395 400

Ala Pro Leu Pro Thr Gly Val Glu Thr Phe Thr Ser Phe Tyr Leu Ala
405 410 415

Ile Thr Ala Asn Pro Arg Arg Gly Arg Phe Thr Trp Asn Pro Glu Ala
420 425 430

Gly Arg Val Glu Leu Asp Trp Arg Gln Glu Trp Lys Gln Pro Ser Val
435 440 445

Asp Met Ala Arg Thr Ile Phe Asp Arg Ile Asn Ser Val Glu Gly Thr
450 455 460

-continued

Val Tyr Arg Ala Asp Leu Phe Gly Ala Gly Lys Val Trp Gly Asp Gly
 465 470 475 480

Leu Thr Tyr His Pro Leu Gly Gly Val Val Leu Gly Arg Ala Thr Asp
 485 490 495

Gly His Gly Arg Leu Ala Gly Tyr Arg Gly Leu Tyr Val Val Asp Gly
 500 505 510

Ser Leu Ile Pro Gly Asn Thr Ser Val Asn Pro Phe Val Thr Ile Thr
 515 520 525

Ala Leu Ala Glu Arg Asn Leu Ala Arg Ile Val Ala Arg Asp Leu
 530 535 540

<210> SEQ ID NO 47

<211> LENGTH: 528

<212> TYPE: PRT

<213> ORGANISM: Chryseobacterium gleum

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (142)..(142)

<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
 Tyr, Lys or Ser

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (211)..(211)

<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
 Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (380)..(380)

<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
 or Asp, provided that when Xaa142 is Met, then Xaa380 is not Phe

<400> SEQUENCE: 47

Met Asp Arg Lys Lys Phe Ile Arg Thr Ser Ala Leu Ala Ile Ser Gly
 1 5 10 15

Phe Tyr Phe Leu Gln Ser Gly Leu Leu His Ala Thr Asn Arg Lys Asn
 20 25 30

Ser Leu Glu Lys Glu Asn Ser Asp Ala Pro Ile Val Ile Ile Gly Ser
 35 40 45

Gly Tyr Gly Gly Ala Val Ser Ala Leu Arg Leu Cys Glu Ala Gly Lys
 50 55 60

Lys Val Val Met Leu Glu Met Gly Leu Asn Trp Glu Lys Ala Gly Ile
 65 70 75 80

Pro Phe Ser Asn Leu Leu Lys Pro Gly Lys Ser Ser Ala Trp Leu Lys
 85 90 95

Lys Lys Ser Ile Ala Pro Phe Met Asn Ile Phe Ser Leu Thr Pro Phe
 100 105 110

Thr Gly Thr Leu Asp Arg Leu Asp Phe Lys His Ile Asn Ile Trp Val
 115 120 125

Gly Arg Gly Val Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val
 130 135 140

Thr Pro Lys Glu Ser Tyr Phe Arg Glu Val Phe Pro Asp Leu Asp Ala
 145 150 155 160

Glu Arg Phe Tyr Ser His Tyr Phe Pro Leu Val Arg Glu Glu Leu Lys
 165 170 175

Val Asn Val Ile Asp Glu Gln Phe Leu Lys Asp Cys Pro Tyr Tyr Gln
 180 185 190

Phe Thr Arg Val Gly Glu Lys Glu Ala His Lys Ala Gly Phe Lys Thr
 195 200 205

Ile Arg Xaa Pro Asn Val Tyr Asp Phe Lys Tyr Met Glu Lys Glu Phe
 210 215 220

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Arg Asn Glu Val Pro Arg Ser Ala Leu Asn Thr Glu Val Ile Tyr Gly
 225 230 235 240
 Asn Asn Tyr Gly Lys Asn Ser Leu Asp Lys Thr Tyr Leu Arg Lys Ala
 245 250 255
 Leu Glu Thr Gly Asn Leu Glu Ile Leu Asp Leu His Arg Val Gln Thr
 260 265 270
 Val Lys Leu Asn Asp Asp Lys Ser Tyr Thr Leu His Val Arg Gln Ile
 275 280 285
 Asp Thr Ser Gly Ser Val Ile Ala Asp Lys Val Phe Asn Cys Lys Lys
 290 295 300
 Leu Ile Leu Ser Ala Gly Thr Met Gly Thr Leu Gln Ile Leu Leu Gln
 305 310 315 320
 Ser Asn Ala Glu Asn Gly Phe Pro Ile His Glu Lys Ile Gly Lys Asn
 325 330 335
 Trp Gly Asn Asn Gly Asn Phe Met Thr Gly Arg Asn Trp Val Lys Pro
 340 345 350
 Leu Ser Gly Gly Thr Gly Ala Lys Gln Ser Thr Ile Pro Val Gly Gly
 355 360 365
 Ile Asp Asn Trp Asp Asp Pro Glu His Gln Phe Xaa Thr Glu Ile Ala
 370 375 380
 Pro Leu Pro Met Gly Met Asp Val Ala Thr Ala Leu Tyr Leu Ile
 385 390 395 400
 Asn Arg Val Asp Lys Lys Gly Glu Val Thr Tyr Asn Lys Ala Ser Gln
 405 410 415
 Ser Leu Thr Leu Asn Trp Asp Glu Ser Asn Thr Ala Lys Met Lys Glu
 420 425 430
 Asn Ala Gln Tyr Phe Ile Arg Lys Met Asn Lys Ala Asn Gly Thr
 435 440 445
 Arg Ser His Leu Leu Phe Asn Asn Gly Phe Gly Ala Glu Ile Cys Tyr
 450 455 460
 His Pro Leu Gly Gly Cys Val Leu Gly Glu Ala Thr Asn Glu Tyr Gly
 465 470 475 480
 Lys Leu Arg Asp His Glu Asn Leu Tyr Val Leu Asp Gly Ser Leu Ile
 485 490 495
 Pro Gly Thr Ile Gly Val Asn Pro Phe Val Thr Ile Thr Ala Ile Ala
 500 505 510
 Glu Tyr Cys Ile Glu Asn Leu Ile Arg Gln Asn Glu Phe Asn Leu Gly
 515 520 525

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<210> SEQ ID NO 48
<211> LENGTH: 525
<212> TYPE: PRT
<213> ORGANISM: Weeksella virosa
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (139)..(139)
<223> OTHER INFORMATION: Xaa is Met, Phe, Leu, Val, Cys, Ile, Ala, Gln,
   Tyr, Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (208)..(208)
<223> OTHER INFORMATION: Xaa is Val, Met, Ile, Ala, Thr, Lys, Cys, Ser,
   Gly, Glu, Tyr, Pro, Asn, Gln, Trp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (377)..(377)
<223> OTHER INFORMATION: Xaa is Phe, Trp, Ser, Thr, Lys, Ala, Asn, His
   or Asp, provided that when Xaa139 is Met, then Xaa377 is not Phe
  
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<400> SEQUENCE: 48

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Met Asn Arg Lys Ser Phe Ile Arg Lys Thr Ser Leu Gly Leu Gly Gly
1           5          10          15

Leu Phe Leu Tyr Lys Pro Met Ser Leu Phe Ser Lys Thr Lys Pro Lys
20          25          30

Lys Glu Pro Ile Glu Lys Pro Ile Ile Ile Gly Ser Gly Tyr Gly
35          40          45

Gly Ala Val Ala Ala Leu Arg Leu Cys Glu Ala Gly Lys Lys Val Cys
50          55          60

Leu Leu Glu Met Gly Leu Asn Trp Glu Lys Ser Gly Glu Lys Phe Ser
65          70          75          80

Pro Met Thr His Pro Gly Lys Ser Ala Ala Trp Leu Arg Lys Lys Thr
85          90          95

Ile Ala Pro Phe Phe Asn Ile Phe Pro Leu Lys Pro Phe Thr Gly Thr
100         105         110

Leu Asp Arg Leu Asp Tyr Lys Asn Ile Lys Ile Trp Val Gly Arg Gly
115         120         125

Val Gly Gly Gly Ser Leu Val Asn Gly Gly Xaa Ala Val Leu Pro Lys
130         135         140

Lys Asn Tyr Phe Lys Glu Ile Phe Pro Thr Leu Asp Val Asp Leu Phe
145         150         155         160

Tyr Asn Lys Tyr Phe Pro Leu Ala Gln Gln Glu Leu Lys Val Asn Val
165         170         175

Ala Asp Glu Glu Phe Leu Gln Ser Cys Ser Tyr Tyr Lys Phe Asn Lys
180         185         190

Val Gly Glu Lys Glu Ala Gln Lys Ala Gly Tyr Lys Thr Ile Arg Xaa
195         200         205

Pro Asn Val Tyr Asn Phe Lys Tyr Met Glu Ala Glu Tyr Glu Asn Lys
210         215         220

Val Pro Arg Ser Ala Leu Ala Gly Glu Val Ile Tyr Gly Asn Asn His
225         230         235         240

Gly Lys Tyr Ser Leu Asp Lys Thr Tyr Leu Lys Lys Ala Asp Ala Thr
245         250         255

Gly Asn Leu Glu Ile Leu Asp Leu His Gln Val Lys Ser Ile Ala Leu
260         265         270

Asn Ser Asp His Ser Tyr Thr Leu Ser Val Asp Gln Ile Asn Thr Ser
275         280         285

Gly Glu Ile Val Gln Val Lys Glu Met Arg Cys Gln Lys Leu Ile Leu
290         295         300

Ala Ala Gly Thr Met Gly Ser Leu Glu Leu Leu Leu Arg Ser Gln Ala
305         310         315         320

Lys Asn Gln Leu Pro Leu Asp Glu His Ile Gly Lys Met Trp Gly Asn
325         330         335

Asn Gly Asn Phe Met Thr Gly Arg Asn Trp Val Lys Ala Phe Ser Gly
340         345         350

Gly Asn Gly Tyr Leu His Ser Thr Ile Pro Val Gly Gly Ile Asp Asn
355         360         365

Trp Asp Asp Pro Lys Tyr Pro Phe Xaa Ala Glu Ile Ala Pro Leu Pro
370         375         380

Met Gly Met Asn Val Ala Thr Ser Leu Tyr Leu Ile Ile Asn Lys Leu
385         390         395         400

Asp Lys Tyr Gly Glu Val Thr Tyr His Pro Thr Glu Asp Lys Leu Asp
405         410         415

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Leu Lys Trp Asp Leu Ser His Thr Lys Lys Met Lys Glu Asn Ala Arg
420 425 430

His Phe Ile Lys Lys Met Asn Arg Thr Asn Gly Gly Thr Arg Ala His
435 440 445

Phe Leu Phe His Asn Gly Phe Gly His Asp Ile Cys Tyr His Pro Leu
450 455 460

Gly Gly Ile Val Leu Glu Lys Ala Thr Asn Pro Tyr Gly Lys Leu Asn
465 470 475 480

Leu His Lys Asn Leu Phe Val Leu Asp Gly Ser Leu Ile Pro Gly Ser
485 490 495

Ile Gly Val Asn Pro Phe Leu Thr Ile Thr Ala Leu Val Glu Tyr Cys
500 505 510

Ile Glu His Leu Leu Gln Ser Lys Glu Phe Glu Thr Val
515 520 525

<210> SEQ ID NO 49

<211> LENGTH: 28

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 49

ggtaacgggt ggcgcggcgg tggAACCG

28

<210> SEQ ID NO 50

<211> LENGTH: 28

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 50

ggtaacgggt ggctgcgcgg tggAACCG

28

<210> SEQ ID NO 51

<211> LENGTH: 28

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 51

ggtaacgggt ggcgacgcgg tggAACCG

28

<210> SEQ ID NO 52

<211> LENGTH: 28

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 52

ggtaacgggt ggcgaagcgg tggAACCG

28

<210> SEQ ID NO 53

<211> LENGTH: 28

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 53

ggtaacggt ggcttcgcgg tggaaccg

28

<210> SEQ ID NO 54
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation
<400> SEQUENCE: 54

ggtaacggt ggccgtgcgg tggaaccg

28

<210> SEQ ID NO 55
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation
<400> SEQUENCE: 55

ggtaacggt ggcacgcgg tggaaccg

28

<210> SEQ ID NO 56
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation
<400> SEQUENCE: 56

ggtaacggt ggcatgcgg tggaaccg

28

<210> SEQ ID NO 57
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation
<400> SEQUENCE: 57

ggtaacggt ggcaaagcgg tggaaccg

28

<210> SEQ ID NO 58
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation
<400> SEQUENCE: 58

ggtaacggt ggccctggcgg tggaaccg

28

<210> SEQ ID NO 59
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation
<400> SEQUENCE: 59

ggtaacggt ggcaacgcgg tggaaccg

28

<210> SEQ ID NO 60
<211> LENGTH: 28
<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: primer for point mutation
 <400> SEQUENCE: 60

ggtaacggt ggcccgccgg tggAACCG

28

<210> SEQ ID NO 61
 <211> LENGTH: 28
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: primer for point mutation
 <400> SEQUENCE: 61

ggtaacggt ggccaggcgg tggAACCG

28

<210> SEQ ID NO 62
 <211> LENGTH: 28
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: primer for point mutation
 <400> SEQUENCE: 62

ggtaacggt ggcttcgcgg tggAACCG

28

<210> SEQ ID NO 63
 <211> LENGTH: 28
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: primer for point mutation
 <400> SEQUENCE: 63

ggtaacggt ggctctgcgg tggAACCG

28

<210> SEQ ID NO 64
 <211> LENGTH: 28
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: primer for point mutation
 <400> SEQUENCE: 64

ggtaacggt ggcaccgcgg tggAACCG

28

<210> SEQ ID NO 65
 <211> LENGTH: 28
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: primer for point mutation
 <400> SEQUENCE: 65

ggtaacggt ggcgttgcgg tggAACCG

28

<210> SEQ ID NO 66
 <211> LENGTH: 28
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: primer for point mutation
 <400> SEQUENCE: 66

ggtaacggt ggccggcgcgg tggAACCG

28

-continued

<210> SEQ ID NO 67
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 67

ggttaacgggt ggctacgcgg tggAACCG

28

<210> SEQ ID NO 68
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 68

cggttccacc ggcgcggccac cgTTAACCC

28

<210> SEQ ID NO 69
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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28

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28

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28

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28

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cggttccacc gccggggcac cgtaacc

28

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28

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29

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29

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29

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29

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29

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29

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29

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29

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29

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29

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29

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29

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<220> FEATURE:
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<400> SEQUENCE: 104

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29

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29

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<400> SEQUENCE: 107
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<400> SEQUENCE: 113

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29

<210> SEQ ID NO 114
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<400> SEQUENCE: 114

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29

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<400> SEQUENCE: 115

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29

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<400> SEQUENCE: 116

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29

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<220> FEATURE:
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<400> SEQUENCE: 117

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29

<210> SEQ ID NO 118
<211> LENGTH: 29
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<400> SEQUENCE: 118

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29

<210> SEQ ID NO 119
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29

<210> SEQ ID NO 120

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<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 123

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29

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<220> FEATURE:

<223> OTHER INFORMATION: primer for point mutation

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<220> FEATURE:

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29

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<400> SEQUENCE: 128

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<212> TYPE: DNA
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<400> SEQUENCE: 131

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<400> SEQUENCE: 133

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<400> SEQUENCE: 134

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<211> LENGTH: 29
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<220> FEATURE:
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<400> SEQUENCE: 135

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<220> FEATURE:
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<400> SEQUENCE: 137

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<220> FEATURE:
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<210> SEQ ID NO 139
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 139

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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 140

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<220> FEATURE:
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<400> SEQUENCE: 141

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<400> SEQUENCE: 142

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<400> SEQUENCE: 143

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<400> SEQUENCE: 144

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<220> FEATURE:
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<400> SEQUENCE: 146

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29

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<220> FEATURE:
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<400> SEQUENCE: 147

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29

<210> SEQ ID NO 148
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<220> FEATURE:
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<400> SEQUENCE: 148

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29

<210> SEQ ID NO 149
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 149

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29

<210> SEQ ID NO 150
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<220> FEATURE:
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<400> SEQUENCE: 150

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29

<210> SEQ ID NO 151
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<400> SEQUENCE: 151

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29

<210> SEQ ID NO 152
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<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 152

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29

<210> SEQ ID NO 153

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<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 157

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29

<210> SEQ ID NO 158

<211> LENGTH: 29

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 158

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<210> SEQ ID NO 159
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<212> TYPE: DNA
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<223> OTHER INFORMATION: primer for point mutation

<400> SEQUENCE: 159

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<210> SEQ ID NO 160
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The invention claimed is:

1. A cholesterol oxidase mutant modified at one or more amino acid positions selected from:

(a) a position corresponding to position 159 of SEQ ID NO: 1 by substituting the amino acid residue Met with an amino acid residue selected from the group consisting of Phe, Leu, Val, Cys, Ile, Ala, Gln, Tyr, Lys, and Ser or by substituting the amino acid residue Ile with an amino acid residue selected from the group consisting of Phe, Leu, Val, Cys, Ala, Gln, Tyr, Lys and Ser;

(b) a position corresponding to position 228 of SEQ ID NO: 1 by substituting the amino acid residue Val, Met or Ile with an amino acid residue selected from the group consisting of Ala, Thr, Lys, Cys, Ser, Gly, Glu, Tyr, Pro, Asn, Gln, Trp and His; and

(c) a position corresponding to position 396 of SEQ ID NO: 1 by substituting the amino acid residue Phe with an amino acid residue selected from the group consisting of Trp, Ser, Thr, Lys, Ala, Asn, His and Asp, wherein the cholesterol oxidase mutant has at least about 95% sequence identity to any one of SEQ ID NOS: 1-5.

2. The cholesterol oxidase mutant of claim 1, wherein the cholesterol oxidase mutant has a reduced oxidase activity when compared to a wild-type cholesterol oxidase.

3. The cholesterol oxidase mutant of claim 1, wherein the cholesterol oxidase mutant has an oxidase activity that is less than its dehydrogenase activity.

4. The cholesterol oxidase mutant of claim 1, wherein the cholesterol oxidase mutant has a dehydrogenase activity of about 50% or more of a wild-type cholesterol oxidase.

5. A cholesterol oxidase mutant comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 1-5 modified at one or more positions corresponding to position 159, 228 or 369 of SEQ ID NO: 1, wherein the cholesterol oxidase mutant has a reduced oxidase activity when compared to a wild-type cholesterol oxidase.

6. An isolated polynucleotide encoding the cholesterol oxidase mutant of claim 1.

7. A vector comprising the polynucleotide of claim 6.

8. An isolated host cell transformed with the vector of claim 7.

9. A method of assaying cholesterol in a sample, the method comprising the steps of:

contacting the sample with a cholesterol oxidase mutant modified at one or more amino acid positions selected from:

(a) a position corresponding to position 159 of SEQ ID NO: 1 by substituting the amino acid residue Met with an amino acid residue selected from the group consisting of Phe, Leu, Val, Cys, Ile, Ala, Gln, Tyr, Lys, and Ser or by substituting the amino acid residue Ile with an amino acid residue selected from the group consisting of Phe, Leu, Val, Cys, Ala, Gln, Tyr, Lys and Ser,

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- (b). a position corresponding to position 228 of SEQ ID NO: 1 by substituting the amino acid residue Val, Met or Ile with an amino acid residue selected from the group consisting of Ala, Thr, Lys, Cys, Ser, Gly, Glu, Tyr, Pro, Asn, Gln, Trp and His, and (c). a position corresponding to position 396 of SEQ ID NO: 1 by substituting the amino acid residue Phe with an amino acid residue selected from the group consisting of Trp, Ser, Thr, Lys, Ala, Asn, His and Asp; and measuring an amount of the cholesterol oxidized by the cholesterol oxidase, wherein the cholesterol oxidase mutant has at least 95% sequence identity to any one of SEQ ID NOS: 1-5.
- 10.** A method of assaying HDL-associated cholesterol in a sample, the method comprising the steps of: contacting the sample with the cholesterol oxidase mutant of claim 1, wherein the cholesterol is obtained from HDL-associated cholesterol prior to the contacting; and measuring an amount of oxidized cholesterol.
- 11.** A method for assaying LDL-associated cholesterol in a sample, the method comprising the steps of:

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- contacting the sample with the cholesterol oxidase mutant of claim 1, wherein the cholesterol is obtained from LDL-associated cholesterol prior to the contacting; and measuring the amount of oxidized cholesterol.
- 12.** A device for assaying cholesterol, HDL-associated cholesterol and/or LDL-associated cholesterol in a sample, the device comprising: the cholesterol oxidase mutant of claim 1; and an electron mediator.
- 13.** A kit for assaying cholesterol, HDL-associated cholesterol and/or LDL-associated cholesterol in a sample, the kit comprising: the cholesterol oxidase mutant of claim 1; and an electron mediator.
- 14.** An enzyme electrode comprising the cholesterol oxidase mutant of claim 1 immobilized on an electrode.
- 15.** An enzyme sensor for assaying cholesterol, HDL-associated cholesterol and/or LDL-associated cholesterol comprising the enzyme electrode of claim 14 as a working electrode.

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